

Nicotine Impairment: The Adverse Effects of Maternal Cigarette Smoking on Fetal and Neonatal Development

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Abstract

Maternal cigarette smoking can not only adversely affect fetal development but also infant development. It is a risk factor for infant low birth rate, preterm birth, failure to reach fetal milestones, and can perniciously result in abnormal fetal thyroid and lung development, causing abnormal heart rate and respiratory infections and asthma, respectively. Maternal cigarette smoking diminishes the quality and quantity of breast milk, and many mothers who smoke stop breastfeeding sooner than their non-smoking counterparts. Although maternal cigarette smoking is a preventable risk factor, smoking cessation is hugely problematic for many mothers due to nicotine addiction and withdrawal. Nevertheless, the sooner the smoking cessation occurs, the greater the fetus' and neonate's chances of avoiding harmful outcomes. Family and community support is vital in helping pregnant or nursing women to stop cigarette smoking. This mini-review aims to bridge the knowledge gap and summarize findings, providing compelling evidence regarding the benefits of smoking cessation to the fetus and neonate.

Keywords: Cigarette Smoking; Fetal Development; Lactation; Neonate; Nicotine

Abbreviations

LBW: Low Birth Weight

Introduction

Cigarette smoking is a severe public health issue [1]. Despite its well-recognized detrimental effects, the use of nicotine, the main component of cigarette smoke, is widespread among pregnant women [2]. The rate of smoking during pregnancy has decreased only

slightly in the last decade. Prenatal exposure to cigarette smoke negatively affects fetal and infant development [3], mostly if the mother continues to smoke throughout the pregnancy. Most knowledge on the effects of prenatal exposure to nicotine has been gleaned from population studies, measuring adverse outcomes in fetuses and infants of women who have smoked before pregnancy and have quit smoking either in anticipation of pregnancy or at the start of the first, second, or third trimester. Although the deleterious effects of prenatal exposure to tobacco smoke on fetal and neonatal development are apparent, smoking cessation benefits have not been systematically investigated [4,5].

Discussion

Smoking increases the risk of preterm birth

The earliest evidence of cigarette smoking's detrimental effects came about by investigating the causal relationship between tobacco exposure and the high incidence of preterm birth. Babies born prematurely have an enhanced risk for developmental deficits due to the lost final weeks (and months) of pregnancy being carried over to the postnatal period. In addition to low birth weight, premature neonates experience feeding difficulties, breathing problems, hearing or eyesight issues, developmental delays, and in extreme cases, cerebral palsy [6–9].

The causal relationship between cigarette smoking and preterm birth was first described more than fifty years ago. Since then, studies have recognized a dose-response relationship to the number of cigarettes smoked [10,11]. Smoking during pregnancy is a preventable risk factor for preterm birth. Studies investigating the benefits of maternal smoking cessation on preterm birth have indicated that quitting smoking any time before or during the first, second, or third trimester of pregnancy can significantly reduce premature birth risk [12,13].

Soneji, *et al.* (2019) compared the rate of preterm births (< 37 weeks of gestation) between expectant mothers (N = 25,233,503) who smoked cigarettes before pregnancy and who quit smoking at the start of or during pregnancy [13]. The findings revealed that earlier smoking cessation during pregnancy was associated with a lower risk of preterm birth. In contrast, in an Ohio-based study, there was no significant difference in the preterm birth rate between non-smokers and early quitters, as well as non-smokers and women who smoked throughout the first trimester [12]. However, the risk of preterm birth increased in late quitters. Overall, these studies indicate that quitting smoking, preferably early in pregnancy, is associated with a reduced risk of preterm birth and long-term benefits for the neonate.

Smoking impacts development from the fetus to neonate

Although temporally shorter than the fetal period, the first month of life is typically associated with high mortality risk [14]. The fetal environment plays an essential role in programming postnatal development and is, thus, the earliest influencing factor in the neonatal period [15,16]. Fetal neurobehavior—as defined by fetal heart rate, motor behavior, and response to environmental stimuli—is strongly associated with neonatal neurobehavioral development [17].

Several fetal developmental milestones affected by cigarette smoking can impact neonatal health. Nicotine exposure from maternal smoking causes abnormal fetal lung development [18]. The effects have been attributed to nicotine crossing the placenta to interact with nicotinic acetylcholine receptors expressed in the fetal lungs. This altered lung function, manifested as a decrease in forced expiratory flow, persists after birth and can, in the long-term, lead to the development of chronic obstructive pulmonary disease [19,20].

Maternal smoking is also associated with a higher risk of neonatal respiratory infections and asthma [18]. Certain studies have indicated the harmful effects of tobacco exposure on fetal thyroid development [21], fetal heart rate [22], and signs of fetal stress [23]—all of which have consequences in neonatal life.

Understanding the effects of cigarette smoke on fetal and infant growth parameters and the extent to which smoking cessation can prevent or minimize these effects, can be valuable in convincing women to refrain from smoking during pregnancy.

Smoking adversely impacts the neonate through diminished breast milk volume and quality and duration of lactation

The detrimental effects of cigarette smoking do not cease with the successful completion of pregnancy and a live neonate delivery. The effects can be protracted, extending to months after delivery, affecting lactation, and, therefore, the newborn's health.

Breast milk is an ideal nutritional meal for the newborn, and breastfeeding is beneficial to both the infant and the mother [24]. Breastfeeding is a choice, and breastfeeding habits are greatly influenced by cultural, socioeconomic, and demographic variables [25]. Nonetheless, even after removing these confounding variables, cigarette smoking can still compromise the benefits of breastfeeding by affecting the lactation process and composition of the milk produced [26].

In a relatively small study (smokers [n = 153] vs. non-smokers [n = 427]), Giglia, *et al.* (2006) analyzed the relationship between cigarette smoking and breastfeeding behavior. The researchers found that women who smoked maintained significantly shorter durations of breastfeeding than non-smoking mothers [27]. On comparing breastfeeding at 2 weeks, 2 weeks to 6 months, and > 6 months, mothers who smoked were significantly less likely to be breastfeeding between 2 weeks to 6 months postpartum and > 6 months postpartum, with the median duration of breastfeeding being 11 weeks for mothers who smoked vs. 28 weeks for non-smoking mothers [27]. Importantly, nicotine can be secreted into the breast milk of active smokers, affecting the flavor of the breast milk, provoking weaning [28].

Cigarette smoking affects the quality of the breast milk by altering its composition. In a study of 92 mothers (31 smokers), conducted by Agostoni, *et al.* (2003), there was a decrease in total lipid and fatty acid content in the breast milk of smokers [29]. Specifically, a significant reduction in docosahexaenoic acid levels was observed, which persisted in the first 3 months of lactation. Although the results indicate a long-term effect of smoking that persists throughout lactation, the small sample size is the study's key limitation [29]. However, without follow-up on infant development, little can be concluded from these observations. Notably, there was no difference in fatty acid composition in breast milk between mothers who actively smoked and those who had stopped smoking during pregnancy.

In contrast, Vio, *et al.* (1991) found that cigarette smoke's negative influence on breast milk volume is directly linked to a lower infant growth rate [30]. Mothers who smoked had significantly smaller breast milk volumes than their non-smoking counterparts (693 ± 110 vs. 961 ± 120 g/d, $p < 0.0001$), which in turn was reflected by decreased weight gain of the infant [30].

Hopkinson, *et al.* (1992) also noted a similar decrease in breast milk volume in mothers who smoked and had delivered preterm infants [31]. However, no difference was observed in milk composition concerning lactose, calcium, nitrogen, and phosphorus levels, highlighting cigarette smoking's effect on breast milk volume than on breast milk composition [31].

Positive outcomes in neonatal development with smoking cessation

Increasing evidence suggests that the timing of smoking cessation is key to attenuate or even eliminate the harmful effects of nicotine [32]. Abraham, *et al.* (2017) [33] and Brand, *et al.* (2019) [34]—investigating the relationship between maternal smoking during pregnancy and fetal measurements—found a decrease in the harmful effects of nicotine exposure on fetal development if the mother had quit or even reduced cigarette consumption during pregnancy. These findings demonstrated an association between earlier smoking cessation during pregnancy and decreased likelihood of adverse outcomes [33,34].

Cigarette smoking is a known risk factor for infant low birth weight (LBW, <2500 g), an outcome that adversely affects neonatal health [35]. Xaverius, *et al.* (2019) analyzed the influence of smoking on neonatal birth weight. This large-scale study included data from women who had quit smoking before conception (n = 12,701), quit smoking during the trimester (n = 5,039, first; n = 2,068, second), smoked

throughout the pregnancy (n = 27,405), or were non-smokers (n = 136,140). Multivariable logistic regression revealed that the risk of giving birth to LBW infants was not significantly higher in women who quit smoking before pregnancy compared to non-smokers [36].

Notably, the probability of giving birth to LBW infants increased with late smoking cessation during pregnancy. This study's findings indicated that the timing of smoking cessation is equally essential in reducing or even eliminating the negative impact on neonatal health [36]. LBW infants have a higher risk of infant mortality and morbidity, such as sudden infant death syndrome (SIDS), cleft lip, and cleft palate [37], implying an imminent need for developing strategies that help eliminate or reduce LBW.

In a seminal study investigating the effects of maternal smoking during pregnancy on developmental outcomes in the neonatal period, Espy, *et al.* (2011) analyzed the smoking patterns of 304 expectant mothers and correlated these smoking patterns to neonatal outcomes [38]. Neonatal developmental outcomes—such as birth weight, head circumference, attention/orientation score, irritability, and stress dysregulation—were monitored. As women frequently underestimate actual smoking behavior [39,40], self-reported smoking behavior was rigorously assessed and verified using biochemical assays that determined the level of cotinine, a metabolic product of nicotine. The researchers found that prenatal tobacco exposure significantly affected neonatal attention skills. They found no differences in irritable reactivity or stress dysregulation between neonates with and without prenatal tobacco exposure. Moreover, no significant differences were noted in growth indices of birth weight and head circumference between neonates born to mothers who quit smoking early in pregnancy and those who smoked throughout the pregnancy. However, the decreases in birth weight tended to follow a dose-response relationship with every additional cigarette smoked toward the end of pregnancy [38].

Although nicotine products are physiologically metabolized during the neonatal period, their detrimental effects can be evidenced even after the infant's birth and long into childhood [2,41]. In addition to having impaired respiratory, cardiovascular, and neurologic systems, infants exposed to prenatal nicotine tend to exhibit aggressive behavior, have poor concentration, and be more susceptible to future substance abuse [42].

Summary

Overall, cigarette smoking's negative influence on pregnancy, breastfeeding, and the neonate's health can be minimized or prevented by reducing or quitting smoking. The collective data reveal a clear benefit for neonates whose mothers quit smoking early, at the start of the pregnancy or within the first trimester [13,34,36,38].

The factors that promote cessation of smoking in women are multifold and complex. In a systematic review and meta-analysis, Riaz, *et al.* (2018) suggested a higher education level and higher socioeconomic status, among other factors, such as health, demographic, relationship, and psychological well-being as strong indicators of smoking cessation during pregnancy [43].

Nicotine is highly addictive [44]; the difficulty of fighting nicotine addiction must not be depreciated. Thus, public health organizations' future focus should be on providing access to smoking cessation programs for women anticipating pregnancy, expectant mothers, and breastfeeding mothers to help them overcome the addiction [45,46]. Smoking cessation for the duration of pregnancy and lactation, and all mothers-to-be, is the ultimate goal [47].

Conclusion

Prenatal exposure to nicotine from maternal cigarette smoke adversely affects fetal and infant development. The adverse effects are amplified if the mother continues to smoke cigarettes throughout the pregnancy. Maternal cigarette smoking is a known risk factor for infant low birth weight, adversely affecting neonatal health. Maternal cigarette smoking has been associated with a high incidence of preterm births and the failure to reach developmental milestones. Nicotine crosses the placenta to interact with nicotinic acetylcholine receptors expressed in the fetal lungs. Thus, maternal cigarette smoking causes abnormal fetal lung development with a higher risk of

neonatal respiratory infections and asthma and negatively impacts fetal thyroid development and fetal heart rate. The detrimental effects of cigarette smoking continue beyond delivery, affecting lactation and the health of the newborn. Cigarette smoking affects the quality of the breast milk by altering its composition. Women who smoke cigarettes have significantly shorter breastfeeding durations than non-smoking mothers and have significantly lower breast milk volumes than their non-smoking counterparts.

However, maternal cigarette smoking during pregnancy is a preventable risk factor. The negative influence of cigarette smoking on pregnancy, breastfeeding, and the neonate's health can be minimized or prevented by reducing or quitting smoking. The timing of smoking cessation is consequential in ameliorating or eliminating the harmful effects of nicotine. The earlier smoking cessation occurs, the higher the likelihood that harmful effects can be attenuated. It is crucial to note that nicotine is highly addictive, and it is particularly challenging to stop smoking while under the influence of nicotine addiction. Nevertheless, quitting smoking for the duration of pregnancy and lactation should be the ultimate—albeit most challenging—goal, that can be aided by partners, family members, healthcare providers, and community and national public health programs.

Conflict of Interest

The authors declare that this paper was written in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest.

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