

Tobacco Smoke and Pregnancy Outcome: Literature Review

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Abstract

Introduction. Pregnant women have a risk for tobacco smoke both actively and passively. Pregnant women are usually exposed to environmental tobacco smoke (ETS) in various places with different duration of time. Cigarette smoke has a severe effect not only on pregnant women but also on the fetus. **Methods** This is a literature review. Various references were collected from online database including reports, journals, mostly in the last 10 years. The journals were mostly from the scholarly journals.

Results. Tobacco smoke can effect the immunity, hormonal and metabolic system of the pregnant woman, therefore disturbing the growth of the fetus. Tobacco smoke also known to increase the risk of premature birth and reduce gestational age. Tobacco smoke cause several problems in newborn such as respiration distress, low birth weight (LBW), neural disorder, sudden infant death syndrome (SIDS) and congenital anomaly.

Conclusion. The effect of tobacco smoke, actively of passively, have worse outcome for the pregnant women and their babies.

Keyword: *Pregnancy Outcome, tobacco smoke, ETS, LBW, preterm birth.*

Introduction

Smoking pregnant women have an increased risk of having an ectopic pregnancy, spontaneous abortion and other complications leading to pregnancy complications as well as the placenta. The fetus also has the risk of exposure to tobacco smoke, more than thousands of types of hazardous chemicals, especially nicotine, tar and carbon monoxide can have an effect on the fetus and cause unwanted disorders or abnormalities¹.

Environmental tobacco smoke (ETS) is a complex mixture consisting of most of the smoke emitted from the smoker's body, the smoke produced by burning cigarettes and the surrounding air². Exposure of ETS

in pregnant women causes increased levels of carbon monoxide (CO), nicotine and cotinine in maternal serum or urine, in the fetus and in amniotic fluid. The effect of ETS on pregnant women can occur from the first semester to the third semester. Pregnant women are usually exposed to ETS in various places with different duration of time. Places that have the potential to become ETS exposure locations include at home, at work and the outside environment³.

Tobacco smoke and pregnancy

One effect of the cigarette smoke exposure on pregnant women is its effect on the mother's immune system. In pregnancy changes occur in the mother's immune system to prevent rejection of the fetus. Exposure to ETS can cause changes in the immune system of pregnant women. Changes include an increase in activated leukocytes and a decrease in the percentage of regulator T lymphocyte cells (Treg cells). Smoking

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during pregnancy also affects the function balance between Th1 cells (T helper lymphocytes) and Th2 cells, causing an increase in the production of cytokines, proinflammatory chemokines and Th1 growth factors. In addition, the percentage of macrophages and NK cell residues is higher in smokers in the first semester (4)

The activation of nicotine receptors causes the release of acetylcholine, dopamine, serotonin, growth hormones and adrenocorticotrophic hormones and glutamate, these hormones significantly influence fetal growth. Smoking is also associated with changes in metabolism during pregnancy.⁴

Exposure to nicotine in pregnant women can cause vascular placental vasoconstriction, decrease placental blood flow and reduce trophoblast invasion which results in inhibition of good placental circularization leading to placental hypoxia causes disruption of placental invasion. Placenta previa is a form of placental invasion disorder⁴. Nicotine can cause a significant decrease in the mitotic potential of cytotrophoblast tissue in vitro. This effect is also found in smoker women. This effect can explain the mechanism of impaired placental development during the early phases of pregnancy due to placental ischemia which can cause fetal death⁵. Low placental weight strongly related with LBW⁶.

Beside nicotine and cotinin, CO levels are also the found highest in smokers. The presence of CO in the body causes oxygen binding to hemoglobin decrease due to the higher affinity of hemoglobin for CO. CO Exposure to the fetus prevents the release of oxygen and then converted to carboxyhemoglobin. The result is a decrease in tissue oxygenation through competitive inhibition with oxyhemoglobin. Prolonged CO exposure in pregnant women can cause significant permanent damage to the brain of a fetus which sensitive to hypoxia. Nicotine is also considered to have a bad effect due to the stimulation of nicotine cholinergic receptors and their neuroteratogenicity effects.^{4,7,8} Nicotine also interferes with the micro RNA which is important for the maturation of fetal stem cells.⁹

The effects of tobacco smok on the fetus are considered to be multifactorial, including indirect effects such as poor nutritional status associated with anorexiagenic effects of nicotine exposure, and CO. Placental blood flow decrease is associated with the

vasoconstrictive effect of catecholamines released from adrenals and nerve cells after nicotine exposure.¹⁰

Tobacco Smoke and Preterm Birth

In Europe rates of preterm births are reported between 5 - 9%, while in developing countries and the United States the rate of preterm births reaches 12%. The cause of preterm birth is often difficult to determine. Some risk factors associated with preterm birth include excessive distension of the uterus, low economic status and smoking¹¹. Elective preterm birth may be associated with cigarette-related obstetric complications such as placenta previa, placental abruption and impaired fetal growth. Research shows that smoking during pregnancy increases the risk of preterm birth by 25%. The exposure of ETS also specifically has an influence on preterm birth^{12,13}.

Active smoker mothers have been accepted as a risk for preterm birth, for around 14% of preterm births. One mechanism that links cigarette exposure with preterm birth is the CYP1A1 genotype and GST (glutathione S-transferase). Abnormalities in these genes make mothers more vulnerable to exposure to hazardous substances such as cigarette smoke.¹⁴ Cotinin levels as an indicator of cigarette exposure are also strongly related to preterm birth⁴ The danger of non-smoking tobacco is also seen in the research of Munmun et al. Which shows that non-smoking tobacco (chewed and swallowed) increases the risk of preterm birth.¹⁵

There are four mechanisms proposed by Goldstein et al explain relationship between smoking and preterm birth: (a) Decreased maternal appetite caused by smoking leading to a decrease in nutrition for the fetus, (b) vasoconstriction caused by smoking results in decreased blood supply to the fetus, reduced fetal nutritional supply and slowing the release of catabolism results, (c) cigarettes may have a direct effect of toxins on the fetus and (d) increase in fetal CO levels causes reduced oxygen transport capacity and teratogenic properties.^{11,16}

Prostaglandin has been known to trigger labor. Prostaglandin levels such as F2-isoprostane as a marker of oxidative stress are found in the amniotic membrane and amniotic fluid in smokers. F2-isoprostane levels increased 3 times compared to non-smokers. Increased

F2-isoprostone levels is considered as a mechanism that associated smoking and preterm birth. Smoking is also considered to increase the sensitivity of the uterus to contractile hormone. Research by Egawa et al in mice shows that inhalation of cigarette smoke increases the contractile activity and sensitivity of myometrium to oxytocin.^{11,17} Cadmium found in tobacco smoke interacts with calcium and effects myometrial activity. Cadmium may modulate the function of the oxytocin receptors in the myometrium. Increased levels of cadmium in pregnant women are found to be associated with an increased risk of preterm birth.^{11,18} Another condition associated with preterm birth is necrotizing-enterocolitis (NEC)¹⁹

Spontaneous Abortion

Spontaneous abortion or miscarriage is one of the most common pregnancy complications, about 12-26% of known pregnancies. Generally the literature on the relationship between smoking and abortion does not show any consistency although some studies have concluded that smoking can cause abortion. A meta-analysis study by Pineles et al. Showed the relative risk of abortion during pregnancy is 1.32. The risk of abortion increases with the number of cigarettes. One cigarette per day increases the risk of abortion by 1%. Secondary smokers have an 11% increased risk of abortion.²⁰

Tobacco Smoke Effect on Newborn

Various studies provide an overview of the effects of cigarette smoke on fetal growth and development during pregnancy and infant growth and development after birth

Respiratory Disorder

Smoking during pregnancy can cause the newborn's lungs failed to reach maximum function and continues with decreased lung function. Preterm births in most smokers also cause disruption of lung maturation. Diseases caused by these infants include wheezing, bronchitis, hospitalization due to lung infections and asthma in children.²¹

Generally, children who are exposed to nicotine during pregnancy also experience exposure to cigarette smoke in childhood. This raises the question whether the increased risk of asthma is caused by exposure to

prenatal or post natal cigarette smoke. Research by Pattenden et al showed that exposure to cigarette smoke during pregnancy without post natal exposure still shows an association with an increased risk of asthma.^{22,23} Exposure to cigarette smoke pre natal and post natal also shows an imbalance of Th1/Th2 causes susceptibility of airway reactivation.²⁴

The mechanism of exposure to nicotine causes various pathological conditions in the lungs is not yet fully understood, but based on some data it was found that nicotine causes various anomalies in the lungs. Histological studies in animals show goblet cell hypertrophy after nicotine exposure, and it is associated with asthma in the community.^{22,25,26}

Low Birth Weight

Low birth weight babies are the variables most widely studied the effect of smoking mothers during pregnancy or exposure to cigarette smoke in pregnant women on pregnancy outcomes. Data shows that LBW is more common in smokers (12.4%) compared to nonsmokers (7.7%). Women who smoke have a 1.5 to 3.5 times greater risk of giving birth to LBW, and the risk increases along with the cigarette consumption.¹

Lee et al study showed that exposure to ETS in pregnant women also has the potential to cause LBW, and the effect of smoking on LBW from active smokers has the same mechanism as the effect of smoking on LBW in secondary smokers. The risk of small infants according to pregnancy is also increased in the group of mothers with high ETS exposure compared with mothers with low ETS exposure²⁷

Behaviour and Neural Disorder

Nicotine exposure to the fetus can affect fetal brain development¹⁰. A study in Finland shows that heavy nicotine exposure caused the infant born with attention deficit / hyperactivity disorder (AHDH) or attention deficit / hyperactive disorders.²⁸ Fetuses exposed to tobacco smoke during pregnancy were found to have a risk of cardiac autonomic abnormalities during sleep especially in preterm babies. Changes in autonomic activity are at risk of causing neurological and cardiological complications²⁹.

Sudden infant death syndrome (SIDS)

One of the most severe complications of nicotine exposure in pregnancy is sudden infant death syndrome or SIDS. The cause of SIDS is not clearly known in infants less than one year old suddenly die without definite explanation even after a thorough investigation. Exposure to nicotine is known to be a risk factor for SIDS, but the mechanism of nicotine exposure that causes infant death is unclear and is still being debated. But some animal studies provide some clues.^{22,30,31}

Congenital Anomaly

The effects of tobacco smoke on infant congenital anomalies have been investigated. Exposure to tobacco smoke is known to be associated with fetal heart defects including atrial septal defects, atrioventricular septal defects, transposition of large arteries, craniosynostotic cleft palate and gastroschisis.^{4,33}

Conclusion

Tobacco smoke effect the immunity, hormonal and metabolic system in pregnant women. The substance found in tobacco smoke were found to be the cause of some pregnancy complication leading to poor pregnancy outcome such as preterm birth, spontaneous abortion, and adverse effect on the infants. The infants could suffer respiratory disorder, behavior and neural disorder, SIDS and another congenital anomaly. The effect of tobacco smoke, actively or passively, associated with poor outcome for the pregnant women and their babies.

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