

“Effects of Maternal Age, Parity, and Smoking on the Risk of Stillbirth” (1994), by Elizabeth Raymond, Sven Cnattingius, and John Kiely

In April 1994, Elizabeth Raymond, Sven Cnattingius, and John Kiely published “Effects of Maternal Age, Parity, and Smoking on the Risk of Stillbirth,” hereafter “Effects on Stillbirth,” in the *British Journal of Obstetrics and Gynecology*, now known as *BJOG: An International Journal of Obstetrics and Gynecology*. The article examines how advanced maternal age, defined as delivery at thirty-five years old or older, cigarette smoking, and nulliparity, or the state of never having given birth, can negatively impact pregnancy. At the time of publication, according to Raymond and colleagues, stillbirths comprised over half of all perinatal, or close to birth, deaths and more than one-third of total fetal and infant deaths in Europe and North America. In the article, Raymond and her coauthors demonstrate how certain risk factors may increase the risk of stillbirth at different stages of pregnancy, which helped set a foundation for future research in interventions to prevent stillbirth.

Some women experience complications during pregnancy that may impact the pregnant woman's health, the fetus's health, or both. Pregnancy complications may lead to stillbirth, which is the death of a fetus that occurs after twenty weeks of pregnancy, either before or during delivery. Four common pregnancy complications discussed in “Effects on Stillbirth” include hypertensive diseases, diabetes, placental complications, and intrauterine growth restriction, or IUGR. Hypertension, also known as high blood pressure, and diabetes, a metabolic disease that causes high blood sugar, can both threaten the health of the placenta, which provides nutrients and oxygen to the fetus. Disruptions to placental health can harm both the fetus and the gestating parent. Placenta-specific complications include a range of issues, including placental abruption, placenta previa, and other problems involving blood flow to or from the placenta. Placental abruption is when the placenta partially or totally detaches from the inner uterine wall before delivery, and placenta previa is when the placenta totally or partially covers the cervix. IUGR refers to extremely low weight of the fetus, defined as the fetus being smaller than ninety percent of fetuses at its gestational age, or how far along in a pregnancy the fetus is. IUGR indicates that the fetus is not growing at an appropriate rate, which can result in numerous health issues.

Raymond, Cnattingius, and Kiely wrote “Effects on Stillbirth” to address the choice of previous studies to group stillbirth at all stages of pregnancy in one category, which the authors perceived as a shortcoming. The authors sought to study stillbirth of a fetus before delivery separately from other cases of perinatal death, such as death of a neonate shortly after delivery, and studied risk factors affecting likelihood of fetal stillbirth. At the time of the article's publication, Raymond was an epidemiologist at the National Institute of Child Health and Human Development in Rockville, Maryland. Cnattingius was an associate professor of social medicine at Uppsala University in Uppsala, Sweden. Finally, Kiely was an epidemiologist at the Centers for Disease Control and Prevention in Hyattsville, Maryland.

“Effects on Stillbirth” is divided into four sections. In the Introduction, the authors state how they consider stillbirth separate from other forms of infant death and point out that there is a documented higher risk of stillbirth associated with several risk factors such as nulliparity, or having never given birth, advanced maternal age, which they define as being thirty-five or older during delivery, and regular cigarette smoking. In the Subjects and Methods section, the authors describe the process of obtaining birth data and maternal data from the Medical Birth Register of Sweden, which contains a comprehensive medical data set on nearly all pregnant patients and newborns in Sweden. In

the Results section, the authors describe how the effects of the risk factors they investigated vary between different demographic groups and vary based on how far along the affected pregnancy is. Finally, in the Discussion section, the authors provide an explanation as to how the risk factors may impede the development of the fetus and lead to higher stillbirth risk.

In the Introduction, Raymond and colleagues state that advanced maternal age, nulliparity, and cigarette smoking are independently associated with higher risks of fetal death but that previous studies did not explain the clinical mechanisms behind the association between those factors and higher risk of stillbirth. As a result, the authors sought to gather clinical data about how age, nulliparity, and smoking may lead to fetal death. They utilized the Medical Birth Register of Sweden, which documents almost all births in the country along with maternal information, such as age, parity, smoking habits, and previous medical complications. From that population-wide dataset, the authors gathered data on maternal age, parity, and smoking in relation to the timing of fetal death and possible causes of it.

In the next section, Subjects and Methods, Raymond and her team describe how they obtained data for their analysis. They explain that the Swedish Medical Birth Register receives comprehensive information on births from all hospitals in Sweden, and it recorded over 714,000 births between 1 January 1983 and 31 December 1989. The authors then explain the exclusion criteria they used to narrow down the data for their study. First, they restricted the data to citizens whose pregnancy involved a single fetus, excluding cases like twins or triplets. Next, they excluded women who were younger than twenty years old and those whose maternal age was unknown, since the authors sought to focus age-related analysis to advanced maternal age, which they defined as being older than thirty-five years old at delivery. Finally, they excluded births in which the fetus was less than twenty-eight weeks old. Their final study population included around 638,000 deliveries, including over 2,000 stillbirths. The researchers split maternal age into two categories, which were those who were twenty to thirty-four years old at delivery, and those who were thirty-five years old or older. They categorized subjects as either nulliparous, meaning they have never given birth, or multiparity, meaning they have given birth at least once. The researchers included both live births and stillbirths in the number of births. The researchers used information on smoking that had been collected at the woman's first prenatal visit to classify women as non-smoking or smoking at least one cigarette daily. They then performed a statistical analysis to determine the association between maternal characteristics and pregnancy complications.

In the Results section, the authors show that advanced maternal age, nulliparity, and daily smoking were significantly associated with stillbirth risk. The risk associated with maternal age was similar for women at all ages in the twenty to thirty-four range, but rose substantially beginning at thirty-five years old. Pregnancy complications, including diabetes, hypertensive diseases, and placental complications in pregnancy, were significantly more common among women aged thirty-five or older than among women aged twenty to thirty-four. The authors' data also showed that hypertensive diseases, placental complications, and IUGR, or extremely low fetus weight, occurred more commonly in nulliparous than multiparous women. Finally, the authors show that placental complications and IUGR were more common in pregnancies of smokers than nonsmokers.

Continuing in the Results section, the authors investigate how stillbirth risk correlates with gestational age. Gestational age describes how far along the pregnancy is. An average pregnancy lasts from thirty-eight to forty-two weeks. Raymond and colleagues state that the risk of stillbirth increased the further along a pregnancy was, especially for pregnant women over thirty-five years old and pregnant women who were regular smokers. Before thirty-two weeks along in pregnancy, older women were not at significantly elevated risk of stillbirth, but after thirty-two weeks, older women's risk of stillbirth increased to a greater extent than for younger women. For smokers, the risk of stillbirth was the greatest early in the third trimester. For women who had not previously given birth, there was a slightly higher overall risk of stillbirth compared to women who had previously given birth, with the highest risk occurring after week forty of pregnancy, which is typically when birth occurs.

In the Discussion section, Raymond and coauthors offer further explanations for the trends that were shown in the Results section. They state that previous studies showed a correlation between fetal death and smoking. In the authors' analysis, they found that smokers who did not suffer from

placental complications and who did not deliver IUGR infants did not have an increased risk of stillbirth. Therefore, the authors claim that only smokers with additional complications, particularly placental and IUGR complications, were at a higher risk for stillbirth. Additionally, although older women were more likely than younger women to have diabetes, hypertensive diseases, and placental complications, increased risk of stillbirth appeared across the older age group, regardless of the presence or absence of those health concerns. Older women who had none of those conditions had the same significantly elevated risk as older women in the total population. The authors' results expand on the findings of a 1983 study by Richard Naeye, a pathologist at Pennsylvania State University in Pennsylvania, USA, that analyzed 1435 stillbirths and showed significantly elevated stillbirth rates in older pregnant women without either hypertension or diabetes. Raymond and her team also conclude that the risk of stillbirth increases exponentially the further along a woman is in pregnancy.

According to the author's analysis, the overall risks of stillbirth are positively correlated with older maternal age, nulliparity, and smoking. The authors also noticed significant interactions of both maternal age and smoking with increasing gestational age, meaning that the risks associated with advanced maternal age and smoking are not equal at every gestational stage, but present a greater risk at different stages of a pregnancy. Maternal age and smoking during pregnancy both cause impairment of oxygen transfer to the fetus. The impairment from maternal age becomes more severe the further along a pregnancy is, but the effects of smoking decrease with gestational age. The authors suggest that smoking may be especially harmful to the immature fetus and placenta. Raymond, Cnattingius, and Kiely claim that specific attention must be focused on stillbirth as a distinct clinical and epidemiological problem. For example, both advanced maternal age and smoking have been shown to be stronger risk factors for death before birth than for early neonatal death, or death soon after delivery. The article makes a case for why stillbirths should be studied using a more detailed timeline rather than grouped into a single perinatal mortality category, which could span weeks before and after birth of the neonate.

Stillbirth represents one of the most common forms of fetal death in the world. The article from Raymond and her team reveal common risk factors that may increase the risk of stillbirth, and it provides possible interventions that people can take to reduce the risk of it. As of June 2021, the article has been cited over 250 times, with many of the articles further examining perinatal mortality and the common social and medical factors that cause it around the world. Overall, the article provides a framework for further studying the causes of stillbirths, which may aid healthcare facilities in preventing it from happening to pregnant patients.

Sources

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