

Prenatal Cigarette Exposure Increases Risk for Psychiatric Illness Into Adulthood **CME**

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CME Released: 08/05/2010; Valid for credit through 08/05/2011

August 5, 2010 — The risk for psychiatric illness is significantly higher in young adults exposed to cigarette smoke in the womb relative to those without prenatal cigarette smoke exposure, even after adjusting for maternal psychiatric illness and other confounding factors, according to a Finnish study reported in the August issue of the *Archives of General Psychiatry*.

"This association seemed to be robust because it could be found in a large group of diagnoses and the dose relationship was also strong," first study author Mikael Ekblad, BM, of University of Turku, Finland, and colleagues note in the article.

Prenatal smoking exposure impairs fetal growth and modulates brain development, which may alter mental development of the offspring, they point out.

The researchers used population-based, longitudinal registry data to evaluate the effects of prenatal smoking exposure on psychiatric morbidity among 175,869 Finnish young adults born from January 1, 1987, through December 31, 1989, with follow-up lasting 18 to 20 years. They had information on mothers' smoking habits (self-reported) during pregnancy and other relevant background factors, as well as psychiatric history of mothers and offspring.

Smoking during pregnancy was reported by 26,075 mothers (15.3%). Of these, 8866 (34.0%) smoked more than 10 cigarettes a day. In 5487 children (3.2%), maternal smoking history was unknown.

The prevalence of any psychiatric diagnosis was 15.0% after excluding the children with unknown maternal smoking history. The prevalence was 13.7% in unexposed children (the reference group), 21.0% in those exposed to fewer than 10 cigarettes a day (adjusted odds ratio [aOR], 1.53; 95% confidence interval [CI], 1.47 – 1.60), and 24.7% in those exposed to more than 10 cigarettes a day (aOR, 1.85; 95% CI, 1.74 – 1.96).

Prenatal smoke exposure significantly increased the risk for most of the psychiatric diagnoses, with the exception of schizophrenia and anorexia diagnoses, the study authors report. The strongest effects were seen for psychiatric disorders due to psychoactive substance use and behavioral and emotional disorders. The lack of a statistically significant finding for schizophrenia may be due to a fairly low number of cases in the study.

There were 870 total deaths in the study population (5.7 per 1000), of which 64 (7.4%) were suicides (excluding children with unknown maternal smoking data). After adjusting for confounding factors, young adults exposed to >10 cigarettes a day during gestation had a significantly increased risk for early death (OR, 1.69; 95% CI, 1.31 – 2.19) compared with unexposed young adults. The mortality rate per 1000 children was 4.7 for unexposed children vs 6.3 and 9.1 for exposure to <10 and >10 cigarettes per day, respectively.

Results Generally Mirror Prior Studies

Commenting on the study for *Medscape Medical News*, David M. Fergusson, PhD, of the Department of Psychological Medicine, Christchurch School of Medicine & Health Sciences in New Zealand, who was not involved in the study, said, "The results are generally consistent with previous research that has suggested that maternal smoking may be associated with increased risks of at least some mental disorders."

In their report, Dr. Ekblad's team points to several study strengths, including a large national study population; the ability to control the child's outcome for maternal mental illness, which has not been done previously in similar large epidemiologic studies; and adjustment for a wide range of background factors, such as 5-minute Apgar scores, the child's birth weight, maternal age, and the mother's psychiatric morbidity before the child's birth.

Limitations of the study include lack of information on alcohol and illicit drug use during pregnancy; self-reported maternal smoking history; potential concern about accuracy of diagnoses; and lack of socioeconomic data, such as parents' educational level and exposure to passive smoke in the home, which can affect risk for psychiatric problems.

"The study," Dr. Fergusson noted, "adds to previous research by being based on a large population (but) is limited by the use of official record data."

The control of confounding factors is "limited," he added, "raising the possibility that the findings may reflect the presence of other factors, which are associated with pregnancy smoking. A further limitation is that the mechanisms by which pregnancy smoking may lead to increased risks of a wide range of mental disorders are by no means clear."

Nonetheless, Dr. Fergusson said this new study further reinforces public health messages regarding the adverse effects of smoking during pregnancy. "It is well known that pregnancy smoking increases the risk of miscarriage, stillbirth, and low-birth-weight infants. The present findings raise the possibility that exposure to pregnancy smoking may have adverse effects on longer-term mental health of offspring," he noted.

The study was supported by the Turku University Hospital Research Foundation, the Finnish Foundation for Alcohol Studies, and the South-West Finnish Fund of Neonatal Research. The study authors and Dr. Fergusson have disclosed no relevant financial relationships.

Arch Gen Psychiatry. 2010;67:841-849.

Clinical Context

Prenatal smoking exposure has been linked to reduced fetal growth and other harmful effects. Maternal smoking during pregnancy may affect prenatal brain development, which in turn may impair mental development of the offspring in childhood and even into young adulthood.

Previous studies have shown an association of prenatal smoking exposure with an increased risk of internalizing and externalizing psychiatric symptoms in children, with persistence of these symptoms into adolescence. Links have also been shown between prenatal smoking exposure and conduct disorders, antisocial behavior, delinquency, and alcohol and other substance abuse disorders.

Study Highlights

- The goal of this population-based longitudinal study was to examine the effects of prenatal smoking exposure on psychiatric morbidity and mortality among Finnish young adults.
- The source population included all singleton births in Finland from January 1, 1987, through December 31, 1989 (n = 175,869), for which data on prenatal smoking exposure were available.
- Children with major congenital anomalies (3.1%) and children who died during the first week of life (0.3%) were excluded.

- Using the Finnish Medical Birth Register, the investigators obtained data on maternal smoking and other background factors as reported by the mothers.
- Smoking was classified as 0, less than 10, or more than 10 cigarettes daily.
- Background data included maternal age and parity and the child's sex, gestational age, birth weight, and 5-minute Apgar score.
- Using the Finnish Hospital Discharge Register, the investigators obtained data on children's psychiatric diagnoses related to outpatient visits from 1998-2007, children's inpatient care from 1987-2007, and mothers' psychiatric inpatient care from 1969-1989.
- The Cause-of-Death Register allowed determination of children's deaths and their causes.
- Psychiatric morbidity and mortality were the primary study endpoints.
- Prevalence of maternal smoking was in 26,075 mothers (15.3%).
- Compared with the unexposed children, children exposed to prenatal smoking had a significantly higher risk for psychiatric morbidity.
- Any psychiatric diagnosis was present in 13.7% of the unexposed children (reference group), in 21.0% of the offspring of mothers who smoked less than 10 cigarettes a day (aOR, 1.53; 95% CI, 1.47 - 1.60), and in 24.7% of the offspring of mothers who smoked more than 10 cigarettes a day (aOR, 1.85; 95% CI, 1.74 - 1.96).
- The risk for psychoses was significantly higher in exposed vs unexposed children.
- Although the risk for most of the psychiatric diagnoses was significantly increased with smoking, the greatest risks were for psychiatric disorders as a result of psychoactive substance use and for behavioral and emotional disorders.
- Prenatal smoking exposure was associated with an increased risk for all diagnoses except for schizophrenia subgroup and anorexia diagnoses.
- There was a dose relationship in the risk for mood disorders and behavioral and emotional disorders occurring in childhood and adolescence, as well as for disorders of conduct and emotions.
- Compared with unexposed children, children exposed to more than 10 cigarettes a day had a 69% significantly increased risk for early mortality (OR, 1.69; 95% CI, 1.31 - 2.19).
- Both groups had a similar prevalence of suicide, which might be because of the low number of suicides in this study.
- On the basis of these findings, the investigators concluded that prenatal smoking exposure is associated with an increased risk for psychiatric morbidity and that prenatal exposure to more than 10 cigarettes a day increases the risk for mortality in childhood, adolescence, and young adulthood.
- They suggest that it might be possible to reduce psychiatric morbidity by decreasing smoking exposure during pregnancy.
- Limitations of this study include self-report of maternal smoking during pregnancy, which tends to underestimate the true extent of smoking; and diagnoses made in a variety of hospitals.
- In addition, the investigators could not adjust for socioeconomic background factors in early life or for paternal characteristics.

Clinical Implications

- In a large Finnish population-based study using registry data, prenatal smoking exposure was associated with an increased risk for psychiatric morbidity. There was a dose relationship in the risk for mood disorders and behavioral and emotional disorders occurring in childhood and adolescence, as well as for disorders of conduct and emotions.
- In that study, prenatal exposure to more than 10 cigarettes a day was associated with an increased risk for mortality in childhood, adolescence, and young adulthood

