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First trimester smoking linked to oral clefts

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Smoking during the first trimester of pregnancy is clearly linked with an increased risk of cleft lip in newborns. Genes that play a role in detoxification of cigarette smoke do not appear to be involved. This is shown in a new study published in the journal *Epidemiology*.

Oral clefts are one of the most common birth defects. Closure of the lip occurs about 5 weeks into pregnancy, followed by closure of the palate at week 9. If this does not happen, a cleft lip and/or cleft palate are the result, requiring surgery. The researchers wanted to see if smoking or exposure to passive smoking play a role in these defects and whether genes influence the oral cleft risk through the way toxic chemicals in cigarette smoke are processed.

The study is based on an extensive Norwegian case-control study on oral clefts with collaborating researchers from the Norwegian Institute of Public Health, University of Bergen, Rikshospital, Haukeland University Hospital and the National Institutes of Health in USA. Between 1996 and 2001, 676 babies born with oral clefts were referred for cleft surgery, and of these, 573 took part in the study. 763 babies born during the same period in Norway were randomly selected as controls.

Blood samples were taken from the children referred for surgery and their PKU test samples, routinely taken at birth, were also retrieved. Their mothers and fathers donated cheek swabs and blood samples. From the control group, cheek swabs were obtained from the mother, father (after November 1998) and child, plus the PKU test sample taken at birth. DNA was extracted from the samples.

Four weeks after birth, the mothers in both groups completed a questionnaire about medical conditions and environmental exposure. They were specifically asked about their smoking habits and exposure to passive smoking before pregnancy and during the first trimester. 42 % of case mothers and 32 % of control mothers said that they smoked in the first trimester.

There was little evidence of an effect of smoking on the risk of cleft palate alone. However, for cleft lip (with or without cleft palate), there was an increased risk, almost two-fold when the mother smoked over 10 cigarettes per day and a 1.6 fold risk from passive smoking (defined as being within 2 metres of a smoker for 2 hours a day). The researchers estimate that 19 % of cases of cleft lip in Norway may be due to maternal smoking in the first trimester.

Using the DNA extracted from the babies and their parents, the researchers looked at the genes related to detoxification of chemicals in cigarette smoke (NAT1, NAT2, CYP1A1, GSTP1, GSTT1, GSTM1). These genes did not appear to affect the incidence of cleft lip, although there was an inconclusive link with NAT2 and cleft lip risk which was independent of smoking. The mechanism by which maternal smoking increases the risk of cleft lip remains unknown.

Paper: RT Lie, AJ Wilcox, J Taylor, HK Gjessing, OD Saugstad, F Aabyholm and H Vindenes. Maternal Smoking and Oral Clefts. *Epidemiology* 2008: 19 (4) 606-615

Source: Norwegian Institute of Public Health