HDL, Homocysteine Linked to Preterm Birth

These factors may be translated biologically into a higher risk for preterm birth or they are markers.

BY SUSAN BIRK
Contributing Writer

CHICAGO — A prospective study of 5,300 women has provided the first biological evidence of the mechanisms underlying the statistically established association between preterm delivery and the mother's future risk of heart disease and stroke.

Low HDL cholesterol and elevated homocysteine levels surfaced as key factors associated with spontaneous preterm birth, Dr. Michael S. Kramer of McGill University reported in a plenary session at the annual meeting of the Society for Pediatric and Perinatal Epidemiologic Research.

In addition, a significantly higher proportion of women with concentrations of homocysteine above the median showed signs of decidual vasculopathy (13.0% vs. 6.8%), Dr. Kramer said.

The study compared frozen plasma samples and fixed and stained placentas from 207 cases of spontaneous preterm birth with 444 term controls, approximately 2 per case.

Researchers analyzed homocysteine, folate, cholesterol (total, LDL, and HDL), and thrombin-antithrombin complexes and blindly assessed fixed and stained placentas for histologic evidence of infarction and decidual vasculopathy.

Both elevated homocysteine and low HDL cholesterol levels were significantly and independently associated with twice the risk of preterm birth, Dr. Kramer reported. "Similar vasculopathic risk factors may underlie preterm birth and adult coronary heart disease and stroke," he said.

Women who delivered preterm had significantly higher plasma homocysteine (4.0 vs. 3.7 mmol/L; $P = .001$) and lower HDL cholesterol (1.6 vs. 1.8 mmol/L; $P = .0001$) levels, compared with women who delivered at term.

In addition, a higher proportion of women with high homocysteine concentrations (but not low HDL) had decidual vasculopathy (13.0% vs. 6.8%).

"The same factors that we know lead to stroke and heart disease were found to be elevated in the second trimester in mothers who subsequently gave birth preterm," said Dr. Kramer in an interview.

The fact that their placentas showed evidence of vasculopathy on the mother's side was a major finding, because it provides a biological link with the vasculopathic plasma markers, he said.

However, "even if [these results] are robust, we still don't know whether homocysteine and HDL are pathologically involved in a biological sense with the preterm birth, or whether they're just markers of the mother's increased risk," he said.

"In adults, when HDL and homocysteine damage blood vessels, they do it over decades," he said. "With pregnancy, we're talking about months. How do [these factors] get translated biologically into an increased risk for preterm birth? It may be the homocysteine and HDL themselves that are acting on blood vessels in the placenta, or it may be something else that's causing the preterm birth."

Dr. Kramer noted that the differences in HDL and homocysteine levels between the two groups were statistically significant but modest. For example, there was a less than 10% difference between the cases and controls in homocysteine (4.0 vs. 3.7 mmol/L). In addition, "the homocysteine concentrations were not high in terms of what is known or suspected to cause vascular damage, which is why we're underlining the fact that we don't know if it's the homocysteine," he said. "These were not the sky-high levels associated with very high risks of coronary heart disease."

The findings need to be replicated to determine whether they are robust, Dr. Kramer said. "However, I think it's unlikely that they were just a statistical fluke, because they were in the direction you'd expect," he said.

Existing serum banks for large populations would offer a relatively easy and inexpensive method of linking pregnancy outcomes with HDL and homocysteine concentrations, he said. ■

People Born Preterm Are at Risk for Medical, Social Disabilities as Adults

BY MARY ANN MOON
Contributing Writer

The risk of serious medical and social disabilities in adulthood increases sharply with decreasing gestational age at birth, according to a report in the New England Journal of Medicine.

Even young adults who were born preterm but have no lingering medical disabilities are at high risk of failing to complete high school, earning a low income, and failing to marry or have children, said Dr. Dag Moster of the University of Bergen (Norway) and his associates.

The researchers assessed the relationship between gestational age at birth and outcomes in adulthood because "the increased prevalence of medical disabilities, learning difficulties, and behavioral and psychological problems among surviving preterm infants has raised concerns that these infants may have difficulties in coping with adult life."

The authors also observed a significant association of autism spectrum disorders with very low gestational age, but urged caution in interpreting this finding.

They examined the issue using data from compulsory national registries of birth, education, job-related income, disability payments, and criminal records, tracking a cohort of 867,692 people born during 1967-1983 and followed until when they were aged 20-36 years.

The risk of serious medical disabilities such as cerebral palsy, blindness or severely impaired vision, hearing loss, and epilepsy increased markedly with decreasing gestational age, as did the risk of mental retardation and psychological, behavioral, and emotional disorders.

"At 19-35 years of age, nearly 1 of 9 persons who had been born at 23-27 weeks of gestation received a disability pension, as compared with 1 of 12 who had been born at 28-30 weeks, 1 of 24 born at 31-33 weeks, 1 of 42 born at 34-36 weeks, and 1 of 59 born at term," Dr. Moster and his associates said (N. Engl. J. Med. 2008;359:262-73).

Even when people with residual medical disabilities were excluded from the analysis, a lower gestational age at birth was associated with a reduced likelihood of completing high school or higher education and of earning a high income. It also was linked to a low likelihood of finding a life partner and of having children.

"We also observed a significant association of autism spectrum disorders with very low gestational age," but "caution is warranted interpreting this finding given the small number of cases in the very premature groups," the researchers noted.

These results are consistent with those of other studies showing a link between preterm birth and "specific difficulties in the areas of motor, cognitive, behavioral, psychological, and social function among preschool and school-aged children," Dr. Moster and his colleagues said.

The adverse outcomes in adulthood "may represent long-term effects of subtle brain dysfunction caused by preterm birth," or they may be related to biologic and social factors underlying both the preterm birth and its later sequelae, they added.

Despite their study's findings on disability prevalence, the researchers wrote, "It should be recognized that a large proportion of the adults who were born prematurely and did not have severe medical disabilities completed higher education and seem to be functioning well." ■

Flax Oil Ingestion Is Tied to Higher Risk of Preterm Birth

BY ROBERT FINN
San Francisco Bureau

MONTEREY, CALIF. — Ingestion of flax oil by women during the second and third trimester of pregnancy is associated with almost a threefold increase in the rate of premature birth, according to the findings of a recent study.

The format of the study questionnaire did not allow investigators to estimate the dose of flax oil associated with preterm birth, study investigator Anick Bérard, Ph.D., of the University of Montreal said in an interview.

Dr. Bérard noted that the question about flax referred specifically to flax oil, which is often used for constipation during pregnancy, and not flax seed, a common foodstuff.

The investigators found no link between premature birth and ingestion of a number of other herbal products, including chamomile, peppermint, and green tea, wrote lead author Krystel Moussally, B.Sc., of the University of Montreal, and her colleagues in a poster presentation at the annual meeting of the Teratology Society.

The case-control study involved 3,354 women listed in the Quebec Pregnancy Registry who responded to a questionnaire. All gave birth to a live infant between 1998 and 2003 in Quebec hospitals and all were continuously insured by the Regie de l'assurance maladie du Québec drug plan for at least 12 months before and during pregnancy. In all, the investigators mailed 8,505 questionnaires, so the response rate was 39%.

Among the women who returned questionnaires, 22% had given birth before 37 weeks' gestation.

As expected, women who gave birth prematurely differed from the controls on a number of variables.

For example, they were more likely to have asthma, and they had fewer prenatal visits.

After controlling for health status, sociodemographic characteristics, lifestyle habits, medication use before and during pregnancy, pregnancy complications, and the baby's sex, the investigators found that women who used flax oil during their last two trimesters were 2.76 times more likely to give birth prematurely than were those who did not.

"Flax use should be avoided during pregnancy," the investigators concluded. "Caution in the use of not-as-yet regulated [herbal products] during the last two trimesters of pregnancy is warranted."

The investigators stated that they had no conflicts of interest to declare. ■