

Cancer diagnosis while pregnant should not lead to treatment delay or end of pregnancy

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Women who are pregnant when diagnosed with cancer can start treatment for their disease immediately and do not need to terminate their pregnancy due to worries over the effects of therapy on the development of their child.

In a special session on cancer in pregnancy at the 2015 European Cancer Congress on Monday, Professor Frédéric Amant said that new results from a study of 129 <u>children</u>, aged between one and three, born after <u>prenatal exposure</u> to cancer treatment, showed normal development of their mental processes and <u>heart function</u> when compared to a matching group of children from the general population.

"Our results show that fear of cancer treatment is no reason to terminate a pregnancy, that maternal treatment should not be delayed and that chemotherapy can be given. The study also shows that children suffer more from prematurity than from chemotherapy, so avoiding prematurity is more important than avoiding chemotherapy," said Prof Amant, who is a gynaecological oncologist at the University Hospitals Leuven (Leuven, Belgium) and at Antoni van Leeuwenhoek (Amsterdam, The Netherlands). The study is being published simultaneously in the *New England Journal of Medicine*.

A total of 129 children from Belgium, The Netherlands, Italy, and the Czech Republic were included in the study and were matched with a similar number of children of the same gestational age who were born to mothers unaffected by cancer. The children's general health and mental



development were examined when they were 18 months and three years old. At the age of three, 47 of the children also had the functioning of their hearts checked with electrocardiograms (ECGs) and echocardiography.

The most common cancers among the mothers were breast and haematological cancers, such as leukaemia and lymphoma. Eight-nine (69%) of the children were exposed to chemotherapy before birth, four (3.1%) to radiotherapy, seven (5.4%) to both chemo- and radiotherapy, one (0.7%) to trastuzumab, one (0.7%) to interferon β and 13 (10.1%) to surgery alone, while 14 (10.9%) mothers did not receive treatment during pregnancy.

"Compared to the <u>control group</u> of children, we found no significant differences in mental development among children exposed to chemotherapy, radiotherapy, surgery alone or no treatment," said Prof Amant. "Nor was the number of chemotherapy cycles during pregnancy, which ranged from one to ten, related to the outcome of the children."

On a scale for measuring mental development (Bayley Scales of Infant Development), both groups of children had a median average score of 101, ranging between 56-145 in the children exposed to cancer treatment and 50-145 in the unexposed children (the higher the score, the better). Children exposed to chemotherapy had a median average score of 100 versus 99.5 for the control children; those exposed to radiotherapy scored an average of 102 versus 105, to surgery alone, 111 versus 102, and to no treatment, 105 versus 97.5.

However, the researchers found that the scores tended to increase by an average of 2.2 points for every week in gestational age, after controlling for age, gender, country, ethnicity and parental education level. "Delayed development of mental processes appeared to be related to premature birth," he said.



Premature birth was more frequent among children born to mothers with cancer, regardless of whether or not they received prenatal treatment, than in the general population in the countries participating in the study. They had a median gestational age of 36 weeks, ranging from 27-41 weeks; 79 (61.2%) children were born at less than 37 weeks, compared to 7-8% in the general population.

"In most cases, they were born prematurely due to a medical decision to induce preterm so as to continue cancer treatment after the delivery," said Prof Amant. "In some cases preterm delivery was spontaneous and it is possible that cancer treatment plays a role in this. But we do not know what exactly triggers preterm delivery. It could be that chemotherapy induces preterm contractions or vaginal inflammation with preterm rupture of the membranes."

Of the 47 three-year-olds who had their cardiac functioning checked, 29 had been exposed to chemotherapy, but compared to the control group of children, there were no differences or abnormalities.

In 2011, Prof Amant reported results of 70 children born after being exposed to cancer treatment, and this latest report is a continuation of this work. However, now the researchers have a control group of children against which to compare the development of the study children. "We did not have this comparison before. In addition, we have included children born to mothers who had surgery alone, or a diagnosis but no treatment. These latest results are again reassuring, but given that we have a larger group of children and the comparison with the control group, the current data are much more robust," he said.

However, he warned that the results had some limitations. "Our data include many types of chemotherapy, but we cannot guarantee that all types of chemotherapy are safe.



"We need to look at larger numbers of children and larger numbers exposed to each drug in order to be able to document the potential effects of individual drugs. In addition, we cannot extrapolate to newer drugs, including targeted drugs. We need longer follow-up to see if there are any long-term toxic effects in cases where cisplatin was administered before birth. For these reasons we will continue to follow these children until the age of 18 years and we will enlarge the group. This will allow us to document longer-term effects and to draw conclusions for specific drugs. In addition we will investigate to what extent anti-cancer drugs are diluted in the body during pregnancy, and also at the psycho-emotional needs of mothers and their partners."

The mothers with cancer were recruited into the study from the International Network on Cancer, Infertility and Pregnancy registry; they were registered between 2001 and 2014 at the time of their cancer diagnosis. All study children were seen between 2005 and 2015. The control children, because they needed to be matched to the study children, were recruited and examined between 2012 and 2015.

Professor Peter Naredi, the ECCO scientific co-chair of the Congress, who was not involved in the research, commented: "These latest results should be reassuring for pregnant women who have been diagnosed with cancer and who will, naturally, be worrying about the best course of action not only for themselves but for their unborn child. While further follow-up of these children is required, the important message at this stage seems to be that doctors should not only start <u>cancer treatment</u> immediately, but should also try to maintain the pregnancy to as near full term as possible."

More information: "Pediatric outcome after maternal cancer diagnosed during pregnancy" by Frédéric Amant et al. *New England Journal of Medicine*, DOI: 10.1056/NEJMoa1508913. Published online at: www.nejm.org/doi/full/10.1056/NEJMoa1508913.



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