

## Studies reveal associations between pregnancy, breastfeeding, breast cancer and survival

## March 25 2010

Barcelona, Spain: Women who are diagnosed with breast cancer in the 12 months after they have completed a pregnancy are 48% more likely to die than other young women with breast cancer according to new research to be presented at the seventh European Breast Cancer Conference (EBCC7) in Barcelona today (Friday).

However, the study of 2,752 <u>breast cancer</u> patients by Australian researchers found that if the breast cancer was diagnosed while the <u>women</u> were pregnant, their risk of dying was nearly the same as other, non-pregnant women diagnosed with breast cancer - only three percent higher.

Assistant Professor Angela Ives, a research fellow at The University of Western Australia, will tell the conference that the findings suggest that the cumulative effect of pregnancy may play a role in breast cancer prognosis and this, along with whether a woman breast feeds, needs further investigation.

However, she said: "It is important to stress that our findings should not discourage women from <u>breast feeding</u> as we know that this is beneficial to both mother and baby in a number of ways. While most breast symptoms or abnormalities identified in young women are benign, it is important that when a woman is pregnant or breast feeding any symptoms or abnormalities are not assumed to be due to the pregnancy



or breast feeding, particularly if the symptoms persist. It is important that both health professionals and young women are breast aware, even during pregnancy and breast-feeding, and promptly have symptoms investigated to allow early diagnosis.

"For women who are diagnosed with breast cancer after pregnancy, they and their clinicians may wish to consider different forms of treatment to improve survival."

Prof Ives said that because very little is known about gestational breast cancer (breast cancer that is diagnosed while a woman is pregnant or up to 12 months after completion of a pregnancy, including terminations or miscarriages) she and her colleagues decided to find out more so that women could make informed choices about their breast cancer management and pregnancy outcome.

Using the Western Australia Data Linkage System, they identified a group of 2,752 women, aged less than 45, diagnosed with breast cancer in Western Australia between January 1982 and December 2003. They followed them to December 2007 or to their date of death, if earlier.

"The WA Data Linkage System is one of only five comprehensive record linkage systems in the world. It brings together population-based hospital morbidity data, birth and death records, mental health services data, cancer registrations and midwives' notifications, linked back to 1980. In this case we have been able to identify all cases of gestational breast cancer diagnosed in WA and all other cases of breast cancer in similar aged women to identify what is different about them," she said.

The researchers took account of additional factors such as age at diagnosis, histological tumour grade, stage of disease and whether the cancer had spread to the lymph nodes. From the total number of women, 182 were diagnosed with gestational breast cancer, 55 while they were



pregnant and 127 after the end of the pregnancy. Prof Ives found that, as might be expected, histological tumour grade, disease stage and lymph node involvement were all associated with a worse survival for all the women. The finding of the increased risk of death if breast cancer was diagnosed after pregnancy remained after adjusting for lymph node status, disease stage at diagnosis, histological tumour grade and age.

Prof Ives said: "It has been assumed over many years that actually being pregnant at diagnosis led to poor survival, but this study has shown that it might be the amount of time that a woman is pregnant and her body's responses to being pregnant that encourage the growth of a breast cancer. Another explanation might be that the changes in the breast while pregnant and then breast feeding mask a breast cancer, which is, therefore, more advanced when it is diagnosed. It could be a combination of both. In addition, we do know that pregnancy and breast-feeding reduce the long-term risk of a woman developing breast cancer, but we also know that, in the short term, having been pregnant may increase the risk of developing breast cancer. There needs to be further research into these possible explanations for our findings."

Prof Ives and her colleagues are now investigating what might be happening at cell level with the way tumours grow (angiogenesis) and the role played by the body's immune response. They are also carrying out further research on the cumulative effect of pregnancy and breast-feeding and time from conception to date of cancer diagnosis on survival.

In a second study [2], Dr Salma Butt (M.D. and a PhD student at the Department of Surgery, Malmö University Hospital, Sweden) examined the link between the length of time that women breast-fed and the different types of breast cancer they subsequently developed. She found that although the risk of developing breast cancer was the same regardless of the duration of breast-feeding, women who had breast-fed



for six months or longer had a statistically significant risk of developing more aggressive types of breast cancer. However, Dr Butt and her colleagues do not know yet whether this means that these women are more likely to die from their cancer.

Dr Butt said: "Several previous studies have investigated the association between breast-feeding and breast cancer risk, but, to our knowledge, no studies have investigated breast-feeding and risk associated with different types of breast cancer. Furthermore, no study has investigated the association between breastfeeding, types of breast cancer and survival yet.

"Our findings need be followed by studies on survival to see if these more aggressive breast tumours actually lead to a higher death rate or not, because we do know that breast cancers that do not have aggressive characteristics can also have high rates of mortality if they are diagnosed late. This is something that we intend to study next."

Dr Butt and her colleagues examined data collected prospectively from a group of 17,035 women in The Malmö Diet and Cancer Study. They evaluated 622 cases of breast cancer for a range of factors that indicated how aggressive the tumours were (e.g. invasiveness, tumour size, axillary lymph node status, HER2 status, Ki67, which is an indicator for tumour proliferation, etc). They analysed the duration of breast feeding for each child, total amount of time a woman had breast-fed, and the average time of breast-feeding per child; the average duration of breast feeding was divided into four groups: less than 2.2 months, less than four months, four months or more, and 6.2 months or more.

Dr Butt said: "We found a statistically significant risk of grade III tumours in women with an average time of breast-feeding of 6.2 months or more. The risk of tumours expressing higher levels of Ki67 was also significantly associated with longer duration of breast-feeding. We



concluded that long duration of breast-feeding was associated with more unfavourable types of breast cancer."

She stressed that these findings should not discourage women from breast-feeding as there were several strong studies that showed that breast-feeding could reduce a woman's overall risk of breast cancer, and that longer breast-feeding times were good for both mother and baby.

"The most important thing would be to identify women with a higher risk of aggressive types of breast cancer and offer them intensified screening, in order to identify their tumours early."

She said the study was an epidemiological one that could show risk associations but not causes. "The biological mechanisms behind this are still to be identified. What is known is that breast-feeding reduces the number of ovulatory menstrual cycles over a lifetime, thereby reducing the impact of hormone levels present during normal menstrual cycles and, in particular, reducing the progesterone exposure. This may explain the finding in previous studies of a reduced risk of breast cancer in women who had breast-fed. However, breast-feeding stimulates the production of prolactin, a hormone that has been reported to have tumour-promoting effects. But the relation between breastfeeding, prolactin and breast cancer is complex and not fully understood."

## Provided by ECCO-the European CanCer Organisation

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