Pregnancy After Breast Cancer Appears Safe

By Gunjan Sinha

Physicians have often assumed that pregnancy after breast cancer increases the risk of cancer recurrence. But research presented at the eighth European Breast Cancer Conference in March adds to the growing evidence that this assumption is wrong.

In a retrospective analysis, Hatem Azim, M.D., a medical oncologist at the Jules Bordet Institute in Brussels, Belgium, reported that 333 women who became pregnant at any time after being diagnosed with breast cancer had no higher risk of recurrence than that of a control group of 874 breast cancer patients who did not become pregnant. All women in the study group were monitored for an average of 4.7 years after becoming pregnant. The study was the first to look at estrogen receptor (ER) status in particular. Women with ER-positive (ER+) breast cancers who became pregnant had no higher risk of cancer recurrence than that of women with ER-negative (ER−) cancers.

That pregnancy did not increase the risk of women with ER+ breast cancer relapsing is especially significant, said David Cameron, M.D., professor of oncology at the University of Edinburgh, Scotland.

“If pregnancy were to increase the chance that breast cancer would recur because of high levels of estrogen, one would expect to see increased risk only in women with ER+ breast cancer, and one does not in this study. It’s a very important study.”

Azim’s study also implicitly suggests that aborting a pregnancy does not affect breast cancer recurrence. Some studies have found that treating physicians advise up to 35% of women who become pregnant after breast cancer to have an abortion (e.g., J. Clin. Oncol. 2001;19:1671–5 and 2003;21:4184–93). Sometimes the pregnancies may simply have been unwanted. Not all the studies reported why the patient was so advised, Azim said. Regardless of the reason for abortion, “our data suggest no therapeutic role of abortion.”

Previous Studies

Although women diagnosed with breast cancer during their childbearing years represent only 5%–7% of all breast cancer cases, understanding the risks of pregnancy after breast cancer has become more important as more women delay childbearing.
“We see more and more women diagnosed with breast cancer before completing their families,” Azim said. “We should have sound evidence with which to counsel these women on pregnancy.”

Few studies have assessed whether pregnancy increases the risk of breast cancer recurring. Of those that have been done, the data were biased, said Azim. In January 2011, Azim and his colleagues published in the *European Journal of Cancer* a meta-analysis of studies that looked at whether pregnancy increased the risk of breast cancer recurrence. The analysis included 14 published studies, three of which contained data on individual patients. Women who became pregnant tended to have a better overall survival than that of the control group.

However, no study controlled for the lag between breast cancer diagnosis and pregnancy: Women in the study group were matched to control subjects with similar disease stage, age, and other disease characteristics, but not for the number of years they had been disease free after treatment. This meant that for any given case patient in the study, her age-matched control subject may have not become pregnant simply because she relapsed before she could become pregnant, which would bias the data in favor of the study group.

### Addressing Study Bias

To address bias, Azim and colleagues matched each case patient to control subjects who had been relapse free for a period roughly equivalent to the time between breast cancer diagnosis and pregnancy of the matched case. This step was in addition to matching cases according to tumor size, whether axillary lymph nodes were involved, ER status, age, and type of treatment received. However, because the study was retrospective, controlling for the healthy mother effect—the idea that only women who feel healthy give birth—wasn’t entirely possible.

“If these women were working with the concept that getting pregnant would increase the chance of their breast cancer coming back, there is the possibility that women who allowed themselves to get pregnant had a lower risk of breast cancer,” Cameron said. That is, the women who got pregnant may have felt healthier because they had lower risk of breast cancer recurrence in the first place than those who did not become pregnant. “This type of bias is true for any retrospective study, and this is why one can’t really say that the study is definitive,” Cameron added.

Pregnancy after breast cancer is different from pregnancy-related breast cancer. The latter is defined as breast cancer diagnosed during pregnancy or breastfeeding, typically up to 1 year after pregnancy. Although pregnancy-related breast cancers are rare and data on outcomes are scarce, some evidence suggests that breast cancer during pregnancy or lactation behaves more aggressively. The reason is unclear.

“Breast cancer may simply behave differently in different contexts,” said Cameron.

### Long-Term Protectiveness

Azim and his colleagues also found that breast cancer patients who became pregnant had a lower risk of death than that of their matched control subjects, regardless of ER status. This finding is in line with the epidemiological evidence showing that the more children a woman has, the lower her risk of breast cancer. This risk, however, varies with age. Women who bear children before age 30 years have a lower lifetime risk of being struck with breast cancer than that of women who never bear children. Women older than 30 years have a higher risk for the first 4-6 years after bearing a child than that of their child-free peers. After that, however, their lifetime risk also diminishes compared with that of their child-free peers.

Researchers do not yet fully understand the biological mechanisms that confer these protective effects. Animal studies suggest that fetal antigens boost a pregnant animal’s immune system, which may partly explain why pregnancy may be protective, said Olivia Pagani, M.D., a medical oncologist at the Institute of Southern Switzerland in Bellinzona. And although estrogen can fuel tumor growth, some cancers are treated with high doses of the hormone because it causes cancer cells to undergo apoptosis, Pagani added.

While scientists continue to study how hormones affect breast cancer, cancer clinicians are still searching for better data to help counsel young female patients on pregnancy. Several open questions remain. Whether women should wait a certain minimum time before attempting pregnancy after breast cancer is still unclear. Understanding disease-related psychological issues and pregnancy outcomes would also be useful, Pagani said. She is discussing with the Breast International Group and the North American Breast Cancer Group collaboration the idea of setting up a registry to prospectively follow up with young breast cancer patients and collect data on general health, pregnancy, and pregnancy outcomes. Such a prospective study would also minimize the healthy mother effect bias that is so problematic in retrospective studies. Such questions are timely, Pagani said.

“We need to make oncologists sensitive to this issue. All the studies together clearly show that it’s absolutely no longer justifiable to counsel young patients against pregnancy.”

Breast cancer patients are living longer, which means that more young women will choose to get pregnant after having breast cancer, Cameron added. “The probability of surviving to see your child grow up is higher now than it ever was. This is very reassuring for women.”