Breastfeeding and Triple-Negative Breast Cancer: Potential Implications for Racial/Ethnic Disparities

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Breast cancer, like most cancers, is increasingly understood to be a biologically heterogeneous disease. That biological heterogeneity, in turn, has considerable implications for breast cancer epidemiology, such that separate evaluation of biologically-distinct tumor subtypes may offer greater insight into disease etiology and prognosis. In this issue of the Journal, Palmer et al. present a resource for characterizing the epidemiology of breast cancer subtypes: the African American Breast Cancer Epidemiology and Risk (AMBER) Consortium (1). Through this consortium of studies in African American women, Palmer et al. provide an important opportunity not only to better characterize risk factors for breast cancer in an understudied demographic, but also to identify risk factors for the triple-negative subtype of breast cancer that disproportionately affects this demographic.

Triple-negative breast cancer, defined by a lack of estrogen-receptor, progesterone-receptor, and HER2/neu expression, is an aggressive, poor-prognosis, poorly understood disease subtype (2). Incidence rates for triple-negative breast cancer are higher among African American women than among non-Hispanic white women in the United States within every age category (3). The disproportionate burden of this aggressive disease in African American women may also contribute to noted disparities in breast cancer survival by race/ethnicity (4). In order to address, reduce, and ultimately eliminate these well-documented inequalities, it is important to identify those modifiable factors contributing to the unequal burden of triple-negative disease. To date, however, few risk factors for triple-negative breast cancer have been consistently noted. To the contrary, it has become clear that many of the so-called “traditional” risk factors for breast cancer overall do not impact risk of triple-negative disease (2).

Breastfeeding has been one possible exception in the search for risk factors for this poor-prognosis disease subtype. Several studies have now documented a 25% to 50% lower risk of triple-negative breast cancer in parous women who have breastfed for at least four to six months relative to parous women who have never breastfed (5–9). Results from the AMBER Consortium add further support to these previous findings (1). Although information on breastfeeding duration was not provided by Palmer et al., the authors reported an odds ratio of 0.81 comparing risk of estrogen receptor-negative and, more specifically, triple-negative breast cancer in parous women who ever vs never breastfed. Given that the biological mechanisms underlying this repeatedly observed association have not yet been elucidated, it remains plausible that breastfeeding is simply a correlate for some other causal factor; however, the consistency in the literature regarding the magnitude and direction of the relationship between breastfeeding and triple-negative breast cancer is compelling.

The relationship of breastfeeding to triple-negative breast cancer risk is particularly intriguing when considered in the context of racial/ethnic disparities in this exposure. Previous observational studies of breast cancer risk have noted a lower prevalence of breastfeeding history among African American case patients and control patients relative to their non-Hispanic white counterparts (10,11). Using data from one cohort included in the AMBER Consortium (the Black Women’s Health Study) and the Nurses’ Health Study II, Warner et al. recently reported that the age-standardized prevalence of ever-breastfeeding was 44% in parous African American women relative to 81% in parous non-Hispanic white women (11). Consistent with such observational studies, recent national statistics indicate that the prevalence breastfeeding uptake in new mothers remains markedly lower among African American women (58.9%) than non-Hispanic white women (75.2%), despite recent gains across racial/ethnic groups (12).

Assuming the association between breastfeeding and triple-negative breast cancer risk reported by Palmer et al. is unbiased, generalizable, and reflects a causal protective relationship, how much of the racial/ethnic disparity in triple-negative breast cancer incidence might be attributed to noted racial/ethnic disparities in breastfeeding? As a generalization of the population attributable fraction, the impact fraction is a measure of the proportional reduction of disease that would occur if an observed exposure pattern (ie, breastfeeding prevalence in parous African American women) assumed a counterfactual pattern (ie, breastfeeding prevalence equivalent to that in non-Hispanic white women) (13). The impact fraction for a gain in breastfeeding among parous African American women from 44% (as reported by Warner et al. [11] and consistent with the 43% prevalence in the AMBER Consortium) to 81% (as previously reported for non-Hispanic white women [11]) is equal to 66%. That is, under the aforementioned assumptions, an increase in breastfeeding prevalence of this magnitude would lower the incidence of triple-negative breast cancer in parous African American women by almost two-thirds. Of course, the assumption that breastfeeding is causally protective against triple-negative breast cancer is a nontrivial assumption not yet supported by biological evidence. The vast majority of triple-negative breast cancers,
including all such cancers in nulliparous women, are likely unrelated to breastfeeding history. However, given that the majority of African American women are parous, and given that age-specific incidence rates of triple-negative breast cancer are 50% to 100% greater in African American women than in non-Hispanic white women (3), an impact fraction of 66% has the potential to be of considerable public health significance. There are already a multitude of reasons to encourage women to breastfeed and to encourage the workplace and health care infrastructure that might better support breastfeeding in new mothers. Perhaps additional motivation can be found in the goal of diminishing disparities in triple-negative breast cancer incidence.

Beyond breastfeeding, there remains a need to identify the broader environmental, biological, and contextual factors that contribute to the incidence of and disparities in triple-negative breast cancer. Pooled studies, such as the AMBER Consortium, offer great potential for more detailed investigations into the epidemiology of this poor-prognosis disease subtype. As our understanding of the biological heterogeneity of breast cancer evolves, and as we attempt to subdivide our study populations into more and more homogeneous case groups based on that evolving understanding, such large pooled study resources become increasingly important for advancing epidemiologic knowledge and, ultimately, for impacting public health.

References

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