NIH Public Access
Author Manuscript
Breast J. Author manuscript; available in PMC 2014 December 24.

Published in final edited form as:
Breast J. 2009 ; 15(4): 432–434. doi:10.1111/j.1524-4741.2009.00755.x.

High Proportion of Inflammatory Breast Cancer in the Population-Based Cancer Registry of Gharbiah, Egypt

Amr S. Soliman, MD, PhD[*], **Mousumi Banerjee, PhD**[†], **An-Chi Lo, MPH**[*], **Kadry Ismail, MD**[‡], **Ahmed Hablas, MD**[‡], **Ibrahim A. Seifeldin, MD**[‡], **Mohamed Ramadan, MD**[‡], **Hoda G. Omar, MS**[§], **Aya Fokuda, MPH**[*], **Joe B. Harford, PhD**[¶], and **Sofia D. Merajver, MD, PhD**[**]

[*]Departments of Epidemiology, University of Michigan School of Public Health, Ann, Arbor, Michigan, USA

[†]Biostatistics, University of Michigan School of Public Health, Ann, Arbor, Michigan, USA

[‡]Gharbiah Population-based Cancer Registry, Tanta, Egypt

[§]Tanta Cancer Center, Tanta, Egypt

[¶]Office of International Affairs, National Cancer Institute, Bethesda, Maryland, USA

[**]Department of Internal Medicine, University of Michigan Medical School, Ann Arbor, Michigan, USA

To the Editor

Inflammatory breast cancer (IBC), the most lethal form of breast cancer, constitutes 1–2% of all breast cancers in the United States (1). Breast cancer comprises 352% of women's cancers in the Gharbiah cancer registry (GCR) of Egypt (2). Hospital-based studies from the National Cancer Institute of Cairo University (NCI-Cairo) in Egypt suggested that IBC accounts for 10% of breast cancers (3). However, these estimates lacked confirmation from population-based studies. To remedy this deficit, we performed this study to evaluate the frequency and features of IBC in GCR.

Our initial review of GCR data between 1999 and 2003 showed that IBC did not exist despite the clinical experience with frequent cases of IBC at the GCR and the 10% relative frequency of the disease at NCI-Cairo. A multi-disciplinary group of physicians in Egypt and the United States, who were experienced in the diagnosis and management of IBC, collaboratively developed an 84-item checklist of symptoms, signs, and clinical characteristic suggestive of IBC to facilitate and standardize abstraction of information from medical records. IBC cases were identified using the simplified clinical definition of Merajver and Sabel (4) that used erythema, edema, and peau d'orange as the three main clinical features of IBC. Subsequently, cases were grouped as follows: most-likely IBC exhibited all three features, possible IBC cases had any two of the three symptoms or had peau d'orange only, and non-IBC cases had edema only, erythema only, or had none of

© 2009 Wiley Periodicals, Inc.

Address correspondence and reprint requests to: Amr S. Soliman, MD, PhD, Department of Epidemiology, University of Michigan School of Public Health, 109 Observatory Street, or asoliman@umich.edu.

NIH-PA Author Manuscript
NIH-PA Author Manuscript
NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

these three clinical features. IBC status was based on clinical criteria for IBC diagnosis (erythema, edema, and peau d'orange). The checklist was applied to all cases that had at least one of the three defining features of IBC and missing data was denoted.

The study population had 659 cases, comprising four with most-likely IBC, 69 with possible IBC, and 586 who were non-IBC. IBC proportion was calculated according to two different definitions. Under the most stringent definition, most-likely IBC cases were considered as IBC, the proportion of IBC was 0.6%. Under a definition that both most-likely IBC cases and possible IBC cases were considered as IBC, the IBC proportion was 11.1%.

There was no difference in age, parity, menopausal status, concurrent lactation, or family history between the IBC versus non-IBC groups. Warmth, diffuse enlargement, and nipple retraction were significantly higher among the IBC group compared with the non-IBC group (5.5% versus 0.2% with warmth, $p < 0.01$; 8.2% versus 0.7% with diffuse enlargement, $p < 0.01$; and 60.9% versus 8.2% with nipple retraction, $p < 0.01$, among IBC versus non-IBC groups, respectively). There were no significant differences between the two groups in bruising, palpable mass, or ulceration. The IBC group had 12.5% tumor emboli compared with 3.6% among the non-IBC group ($p = 0.02$). More patients (42.5%) in the IBC group received neo-adjuvant chemotherapy compared with 15.4% in the non-IBC group ($p < 0.01$). While 81.9% of the non-IBC group received surgical resection or radiotherapy (73.4%), this proportion was significantly higher than patients receiving resection or radiotherapy among the IBC group (53.5% and 51.9%, both $p < 0.01$). There was no significant difference between the IBC versus non-IBC groups in tumor grade, angiolymphatic invasion, or adjuvant chemotherapy. IBC cases had higher rate of metastasis (41.7%) compared with 27.8% for the non-IBC group ($p = 0.10$). Hormone receptors were higher in the IBC group than the non-IBC group (36.4% versus 16.7%, $p < 0.01$ for ER; 58.3% versus 36.2%, $p = 0.04$ for PR). After adjusting for warmth and systemic symptoms, nipple retraction was independently and significantly predictive of IBC (OR = 18.8, 95% CI: 9.6–37.7).

For the first time, this population-based study confirmed what hospital-based and anecdotal reports suggested, namely that 11% proportion of IBC in Egypt (3). This IBC proportion in Gharbiah is unequivocally higher than that in the U.S. and most western countries where data are available (1,3). We provide a rigorous method to ascertain and study IBC in other populations.

IBC cases in Gharbiah were statistically more likely to have findings of grave breast cancer such as warmth, diffuse enlargement, nipple retraction, ER/PR negative, tumor emboli, and higher utilization of neo-adjuvant chemotherapy, neither of which was used to define the comparison groups. The finding that nipple retraction is very common in IBC in Egypt warrants further investigation and comparison with other regions of Africa and with migrant North African populations in the United States and Europe. Tumor emboli were statistically associated with IBC but not commonly documented and thus not useful for studies utilizing registries.

As expected, clinical symptoms, including nipple retraction and warmth, were strong predictors of IBC, even after adjusting for tumor emboli, ER and PR status. Among other

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

clinical features, erythema, edema, and peau d'orange had significant associations with IBC because of our criteria for IBC diagnosis. It is important to caution that reliance on histologic tumor emboli may lead to drastic underestimation of IBC incidence in registries, where quality of pathological evaluation may be highly variable. Although the proportion of patients receiving adjuvant chemotherapy was similar among IBC and non-IBC groups, neo-adjuvant chemotherapy, surgical resection or radiotherapy were significantly different between IBC versus non-IBC group. The proportion of IBC patients who received neo-adjuvant chemotherapy was significantly higher than that for non-IBC patients. In contrast, a higher proportion of non-IBC patients received surgical resection or radiotherapy, a consequence of the fact a larger proportion of IBC patients progress during neo-adjuvant chemotherapy or develop metastasis prior to initiation of the radiotherapy. Higher rates of neo-adjuvant chemotherapy among IBC patients were reassuring and an important test of internal consistency, as patients receiving neo-adjuvant chemotherapy are clinically most likely IBC cases, given that neo-adjuvant treatment is the recommended standard treatment for IBC in the United States and Egypt.

Regional variations in IBC proportion may occur due to differences in diagnostic tools, disease definition criteria, or difference in incidence because of diverse residential and environmental exposures. The International Classification of Disease for Oncology (ICD-O-2, 8530/3 for IBC) focusing on both clinical and pathological profiles has been employed in recent epidemiological investigations that examined the large-scale population-based Surveillance, Epidemiology, and End-Results (SEER) which uses the ICD system to collect the data (5). Other studies have used the American Joint Committee on Cancer (AJCC) staging as a guideline for diagnosis of subtypes of carcinomas including IBC (6). Our study focused on a minimal clinical definition amenable to be utilized in population-based studies worldwide.

In summary, this study proved that IBC can be identified from cancer registries in developing countries. Such identification should rely on reviewing breast cancer medical records for specific documentation of peau d'orange, edema, erythema, and tumor emboli. Depending on treatment trends in the region studied, neo-adjuvant chemotherapy, surgical resection, and radiotherapy data can serve as indicators of the consistency of IBC diagnosis. This study supports the reported high proportion of IBC in Egypt in previous hospital-based studies (3). Future efforts to understand the epidemiology of IBC would be facilitated by explicitly adding IBC status to cancer registration forms in population and hospital cancer registries, especially in developing countries where resources for research are limited but disease patterns that differ from developed countries may exist. We provide a method for ascertainment of IBC patients to perform future studies. The characterization of IBC in areas of high incidence may eventually provide opportunities for better understanding of IBC risk factors and for channeling limited treatment resources more effectively.

Acknowledgments

Grant CA77612, the Burroughs Wellcome Fund, the Breast Cancer Research Foundation, and the Department of Defense, R25 CA112383, K07 CA90241, and R03 CA117350, the University of Michigan's Cancer Center Support Grant (5 P30 CA46592) from the National Cancer Institute. The authors would like to thank Yasmin Akdas for her

effort on parts of the statistical analysis. The authors gratefully acknowledge the useful discussions with colleagues attending the NCI-MECC IBC Epidemiology meeting at IARC, Lyon in June 2005.

References

1. Anderson WF, Schairer C, Chen BE, Hance KW, Levine PH. Epidemiology of inflammatory breast cancer (IBC). Breast Dis. 22:2005–2006. 9–23.
2. Freedman, LS.; Edwards, BK.; Ries, LAG.; Young, JL., editors. Cancer Incidence in Four Member Countries (Cyprus, Egypt, Israel, and Jordan) of the Middle East Cancer Consortium (MECC) Compared With US SEER. Bethesda, MD: National Cancer Institute; 2006. NIH Publication No. 06-5873
3. Omar S, Khaled H. Inflammatory breast cancer. INCTR Newlett. 2002; 3:1–3.
4. Merajver, SD.; Goodman, VL.; Sabel, MS. Inflammatory breast cancer: advances in molecular genetics and treatment. In: Bonadonna, G.; Hortobagyi, GN.; Valagussa, P., editors. Textbook of Breast Cancer: A Clinical Guide to Therapy. 3. London: Taylor & Francis; 2006. p. 241-256.
5. Hance KW, Anderson WF, Devesa SS, Young HA, Levine PH. Trends in inflammatory breast carcinoma incidence and survival: the surveillance, epidemiology, and end results program at the National Cancer Institute. J Natl Cancer Inst. 2005; 97:966–975. [PubMed: 15998949]
6. American Joint Committee on Cancer (AJCC). Cancer Staging Manual. 6. New York: Springer; 2002. p. 225-226.

NIH-PA Author Manuscript
NIH-PA Author Manuscript
NIH-PA Author Manuscript