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Original Article

Correlations of Diabetes and the Risk Factors with the Survival of Breast Cancer Patients

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Abstract

Introduction: Diabetes is associated with an increased risk of cancer. Because of the metastatic nature of cancer, the survival of women with breast cancer is decreasing despite receiving various treatments such as chemotherapy, radiotherapy, etc. The aim of this study was to investigate the relationship between diabetes and the risk factors related to the survival of breast cancer patients.

Methods: This was a descriptive-analytical study. Patients were selected via systematic random sampling and then divided into diabetic and nondiabetic groups. Then the 5-year survival rate of patients was compared.

Results: The mean and median for survival were 9.95 and 13.00 years. The risk of death in breast cancer patients positive for estrogen receptor was significantly reduced compared with patients negative for estrogen receptor (HR, 0.314; 95% CI, 0.109–0.907; P = 0.03).

Conclusion: The results of the study indicate that the survival of breast cancer patients in diabetics is not significantly different from non-diabetics. Use of metformin and estrogen receptor positivity is associated with higher 5-year survival rates in women with breast cancer. Therefore, cancer screening programs in high-risk groups, especially in diabetic patients, and hyperglycemic control may affect survival time.

Keywords: Diabetes, Breast Neoplasms, Survival Time, Metformin

Introduction

Cancer is a major public health threat across the world, especially in developing countries. The incidence rate of cancer is increasing due to the prevalence of its risk factors, such as smoking, obesity, and physical inactivity (1). Notably, breast cancer is a more prevalent malignancy among Iranian women and the fourth leading cause of cancer death in the world (2). The number of new cancer cases has remarkably increased and cancer death is predicted to reach over 11.4 million in 2030 across the world, manifesting cancer to be a major cause of death. Based on the scientific reports, up to 40% of cancers could be prevented if the risk factors were decreased (3). The correlation between type 2 diabetes and some types of cancer has been identified, while this diagnostic complexity is remarkably increasing. However, cancer, especially breast cancer, is affected by some risk factors, including diabetes, insulin resistance, obesity, smoking habits, socioeconomic status, age, gender, ethnicity, and hormone receptors such as estrogen and progesterone.

The global prevalence of diabetes as a risk factor for cancer has a message to take the disease more seriously (4). Research has investigated the mechanisms through which diabetes and cancer are associated. Because of the metastatic nature of the disease, the survival of women with breast cancer is decreasing despite receiving various treatments such as chemotherapy, radiotherapy, etc.; on the other hand, if these patients also have diabetes, the complications related to diabetes can cause problems, which are likely to affect the survival of patients. Therefore, control of risk factors, especially diabetes, and careful control of hyperglycemia in these patients will be very important in increasing their survival. The aim of this study was to investigate the relationship between diabetes and risk factors with the survival of patients with breast cancer in cancer treatment centers affiliated with Mashhad University of Medical Sciences.

Materials and Methods

This descriptive-analytical study used data for patients diagnosed with breast cancer who were receiving treatment at the cancer treatment centers. The study population included the women patients diagnosed with breast cancer referred to the chemotherapy and hematology-oncology departments of Imam Reza and Ghaem hospitals, Mashhad, Iran. These patients were followed up to evaluate 5-year survival since diagnosis. The breast cancer diagnosis was confirmed based on the criteria of the International Classification of Diseases (ICD), the American Commission on Cancer, and pathology reports. Diabetes had been diagnosed using fasting blood sugar (FBS) and HbA1c tests.

Results

The prevalence of diabetes in breast cancer patients was 12.7%, and the mean duration of having diabetes was 8.27 ± 4.71 years. The mean survival rates of nondiabetic and diabetic patients with breast cancer were 10.021 and 7.420 years, respectively. To investigate the impacts of diabetes on the survival rate of breast cancer patients in the presence of effective factors, such as age (at menarche, menopause, and the first full-term pregnancy), smoking habits, history of OCP use, BMI, estrogen and progesterone receptors, HER2 and HER2 receptor subtype status, and molecular subtype of cancer (luminal A vs luminal B), the data were fitted in the Cox regression model. However, findings indicated no significant differences between survival time of diabetic and nondiabetic patients (HR, 0.758; 95% CI, 0.431-1.334; $P = 0.34$). Based on the above-mentioned risk factors, mortality risk significantly decreased in patients with estrogen receptor-positive breast cancer compared with those with estrogen receptor-negative tumors ($P = 0.03$). With regard to diabetes-controlling drugs, the Cox regression model indicated that mortality risk was significantly decreased in patients receiving metformin (HR, 0.5; 95% CI, 0.226-0.950; $P = 0.04$). However, insulin injection was not associated with the survival rate of breast cancer patients.

Discussion

In the current research, no significant difference was observed between diabetic and nondiabetic groups in terms of survival rate, which is consistent with Villarreal-Garza et al. (5). Therefore, it seems that diabetes does not affect the survival rate independently. In another study, De Bruijn et al. considered diabetes to be a risk factor for breast cancer and cancer death (6). In a similar study, Currie et al. reported an increased mortality rate associated with cancer, especially breast cancer, in diabetic patients compared with nondiabetic ones (7). Furthermore, the results obtained by Erickson et al. showed a significant reduction in the overall survival rate of the survivors of primary breast cancer with chronic hyperglycemia (8). This discrepancy between our findings and the aforementioned studies might be due to metformin use in diabetic patients with breast cancer, which was observed to increase the survival rate of our subjects. In summary, further investigation is recommended to confirm our findings.

References

1. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA Cancer J Clin* 2015;65(2):87-108.
2. Akbari ME, Sayad S, Sayad S, Khayamzadeh M, Shojaee L, Shormaji Z, et al. Breast Cancer Status in Iran: Statistical Analysis of 3010 Cases between 1998 and 2014. *Int J Breast Cancer* 2017; 2017:2481021.
3. Bray F, Jemal A, Grey N, Ferlay J, Forman D. Global cancer transitions according to the Human Development Index (2008–2030): a population-based study. *Lancet Oncol* 2012; 13(8):790-801.
4. Pandey A, Forte V, Abdallah M, Alickaj A, Mahmud S, Asad S, et al. Diabetes mellitus and the risk of cancer. *Minerva endocrinologica* 2011; 36(3):187-209.
5. Villarreal-Garza C, Shaw-Dulin R, Lara-Medina F, Bacon L, Rivera D, Urzua L, et al.

Conclusion

The high prevalence of breast cancer is an important public health issue. According to the study results, diabetic patients are at risk of developing types of cancer, especially breast cancer, due to drug treatments and the presence of risk factors; therefore, screening is important. Given the increased survival in metformin-treated patients, the importance of treating hyperglycemia in diabetic patients with breast cancer is important. Therefore, early screening of diabetic women by physicians, for faster diagnosis of breast cancer at early stages and timely treatment and prevention of metastasis, can improve their survival.

Given the increased risk of death in patients with metastasis, identifying risk factors and early diagnosis could be effective in increasing the survival of patients with breast cancer.

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- Impact of diabetes and hyperglycemia on survival in advanced breast cancer patients. *Exp Diabetes Res*. 2012; 2012.
6. De Bruijn K, Arends L, Hansen B, Leeftang S, Ruiter R, Van Eijck C. Systematic review and meta-analysis of the association between diabetes mellitus and incidence and mortality in breast and colorectal cancer. *Br J Surg*. 2013; 100(11):1421-9.
7. Currie CJ, Poole CD, Jenkins-Jones S, Gale EA, Johnson JA, Morgan CL. Mortality after incident cancer in people with and without type 2 diabetes: impact of metformin on survival. *Diabetes care*. 2012; 35(2):299-304.
8. Erickson K, Patterson RE, Flatt SW, Natarajan L, Parker BA, Heath DD, et al. clinically defined type 2 diabetes mellitus and prognosis in early-stage breast cancer. *J Clin Oncol*. 2011; 29(1):54-60.