

# Reproductive Health Screening in Women with Autoimmune Diseases

Latisha Heinlen, MD, PhD<sup>a</sup>, Eliza F. Chakravarty, MD, MS<sup>b,\*</sup>

## KEYWORDS

- Autoimmune diseases • Rheumatoid arthritis • Systemic lupus erythematosus
- Breast cancer • Cervical cancer • Human papilloma virus • Preventive health
- Screening

## KEY POINTS

- Advances in treatment of autoimmune diseases have led to a reduction in mortality and increased quality of life for these patients, making issues related to long-term preventive health and aging more relevant.
- Immune dysregulation from immunosuppressant medications or the underlying diseases may affect clearance of viral infections or innate tumor surveillance among people with autoimmune diseases.
- Breast cancer risk does not seem to be increased among women with rheumatoid arthritis or systemic lupus erythematosus compared with the general female population.
- Studies are conflicting regarding the relative risk of invasive cervical cancer in women with autoimmune diseases, but there is concern for increased rates of precancerous lesions, including cervical dysplasia and atypia, for which early treatment may affect the development of invasive cancer.

## INTRODUCTION

It is well known that many systemic autoimmune diseases, including systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), carry a striking female predominance. Reasons for this are thought to be multifactorial, but likely involve interrelationships between female sex hormones and the immune system. Because of this correlation, there is concern about the influence of autoimmune disease on the reproductive health of affected women. Aside from well-studied influences of underlying disease on pregnancy, there remains concern that common triggering factors may

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<sup>a</sup> Division of Rheumatology, Oklahoma University Health Sciences Center, 1100 N. Lindsay Avenue, Oklahoma City, OK 73104, USA; <sup>b</sup> Division of Arthritis and Clinical Immunology; Oklahoma Medical Research Foundation, 825 Northeast 13th Street, Oklahoma City, OK 73104, USA  
\* Corresponding author.

E-mail address: [chakravartye@omrf.org](mailto:chakravartye@omrf.org)

influence the development of both autoimmune disease and hormonal malignancies. There is additional concern that the presence of autoimmunity or chronic immunosuppressive medication may mediate risk of chronic viral infections, including human papilloma virus (HPV), known to cause cervical and other malignancies.

Required reporting of invasive cancers to national cancer registries has allowed the estimation of site-specific malignancies by age, race, and gender in the general population. By studying rates observed in large cohorts of autoimmune diseases, standardized incidence ratios (SIRs; the ratio of observed cancers to those expected based on age and gender norms) can be calculated to study the rates of cancer, including female malignancies, providing an easy reference of relative risk of these malignancies that may influence screening practices. This method has been widely used to study the changes in risk of hematologic malignancies and lymphoma in patients with RA who use tumor necrosis factor (TNF) inhibitor medications.

Given increased survival rates and improved disease management for many patients with RA and SLE, attention to the risks and development of comorbid conditions, including cancer, has become more important for patients and their providers. Relative risks of hormone-based malignancies, as well as the identification of specific disease-related or medication-related risks, are critical when caring for women with autoimmune disease across their lifespan so that appropriate screening and preventive services can be implemented as part of comprehensive health care. Admittedly, many patients with underlying systemic autoimmune diseases see their rheumatologists for management of active disease manifestations, and minimization of medication toxicities and/or visits to primary care or other preventive health services may become less prioritized. It is important to understand the rates of breast and cervical cancers in women with SLE and RA, risk factors for development of malignancies, and appropriate screening procedures. The addition of a primary care provider to the medical team may greatly enhance adherence to preventive screening for cancer as well as other comorbid conditions that could complicate underlying autoimmune disease.

## **BREAST CANCER**

Breast cancer is the most common malignancy seen in the general female population, with approximately 1.7 million cases diagnosed worldwide in 2012. Known risk factors for the development of breast cancer include family history, age, race, parity, breastfeeding, use of exogenous estrogens, alcohol, sedentary lifestyle, and increased body mass index.<sup>1</sup> Given that autoimmune diseases often preferentially affect women and may bear unique relationships with female sex hormones, it is important to understand the relative risk of breast cancer among women affected by these chronic diseases. Several large multinational studies have been performed to compare rates of numerous types of cancers in patients with autoimmune diseases and the general population. For example, it is well known that many autoimmune diseases increase the risk of lymphoma compared with the general population, although the absolute risk remains low.

### ***Breast Cancer and Systemic Lupus Erythematosus***

Several large studies and meta-analyses have been published to examine the SIR of breast cancer in women with SLE. One of the largest studies was performed by the international Systemic Lupus International Collaborating Clinics (SLICC), in which 16,000 patients with SLE from 30 participating centers were followed longitudinally. A total of 180 cases of breast cancer were reported: the average age at diagnosis was 54 years,

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