The Journal of Rheumatology 2023;50:1199–1201
doi:10.3899/jrheum.230082
First Release April 1 2023

The Journal of Rheumatology

Letter

Cervical Cancer Screening Is a Highly Neglected Procedure Among Women With Systemic Lupus Erythematosus

To the Editor:

We read with great interest the article published by Chung et al, which emphasizes the low frequency of guideline-congruent cervical cancer screening (CCS) among women with systemic lupus erythematosus (SLE).[1] An adequate CCS was correlated with the use of immunosuppressants and the presence of a gynecologist, whereas Hispanic ethnicity was negatively correlated.

We would like to make some comments and raise questions to reinforce and deepen the discussion on this issue, considering the important findings reported. We wondered whether the results might have been influenced by the data source used to define the Pap smear frequency among the patients studied. The CCS frequency and date of the last CCS may not have been specifically questioned by the consultant rheumatologist. The CCS frequency and date of the last CCS may not have been specifically questioned by the consultant rheumatologist because CCS is not generally assumed to be a rheumatology-specific issue during regular consultation. With the same question in mind, we recently conducted a similar study with 102 patients with SLE who were regularly followed up at a university hospital in Brazil. The date of the last Pap smear performed and its agreement with the Brazilian recommendations for immunosuppressed patients according to the Ministry of Health and National Cancer Institute (INCA)[2] were obtained using a semistructured questionnaire. In addition to clinical and sociodemographic characteristics, we added questions regarding the reasons for nonadherence to the standardized CCS. The mean age and mean duration of disease were 41 (SD 13) and 13 (SD 8) years, respectively; lupus nephritis was diagnosed in 56% of our patients and 54% were receiving immunosuppressants or biologic therapy in addition to prednisone. Hydroxychloroquine was used by 80% of the patients (Table 1).

We found similar results, including 47% of the evaluated patients with overdue CCS, notwithstanding the methodological differences between the study by Chung et al[1] and ours. Both findings emphasize the low rate of guideline-congruent CCS among women with SLE, even in tertiary hospitals, and reinforce the need for higher awareness of CCS. We did not find any correlation of ethnicity, clinical manifestation, or medication used with CCS adequacy; however, patients with more severe disease who were evaluated for the accrual of permanent damage according to Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index had a higher chance of being adherent to adequate CCS frequency (Table 1), an association not found by Chung et al.[1] The main reasons for nonadherence were difficulty accessing a gynecologist (33.3%) and lack of medical requirements according to the patients (20.6%; Table 2). The first reason is in agreement with

Table 1. Demographic and clinical characteristics of patients with SLE.

	SLE N = 102	Adherent n = 54	Overdue n = 48	*P*
Age, yrs, mean (SD)	41 (13)	42 (12)	41 (14)	0.73*
Race, n/N (%)				
White		22/49 (44.9)	22/45 (48.9)	0.69**
Afrodescendant		27/49 (55.1)	23/45 (51.1)	
Disease duration, yrs, mean (SD)	13 (8)	13 (7)	14 (9)	0.68*
Clinical manifestations, n (%)				
Nephritis	55 (56.1)	31 (58.5)	24 (53.3)	0.45**
Neuropsychiatric	6 (6.1)	3 (5.7)	3 (6.7)	0.88**
Hematologic	41 (41.8)	22 (41.5)	19 (42.2)	0.97**
Arthritis	78 (79.6)	44 (83)	34 (75.6)	0.55**
Serositis	40 (48.8)	22 (41.5)	18 (40)	0.73**
Mucocutaneous	72 (73.5)	41 (77.4)	31 (68.9)	0.20**
SDI score, median (IQR)	1 (0-5)	1 (0-5)	0 (0-2)	0.03***
SDI ≥ 1, n/N (%)	50/99 (50.5)	32/53 (60.3)	18/46 (39.1)	0.03**
Treatment, n (%)				
Hydroxychloroquine	82 (80)	43 (79.6)	39 (81)	0.85**
Prednisone ≥ 5 mg	71 (69.6)	36 (66)	35 (72.9)	0.49**
Immunosuppressant or biologics[a]	55 (53.9)	31 (57.4)	24 (50)	0.45**

* *t* test. ** Chi square test. *** Mann-Whitney *U* test. [a] Azathioprine, cyclophosphamide, mycophenolate mofetil, rituximab, belimumab. SLE: systemic lupus erythematosus; SDI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index.

Table 2. Reasons given by patients with SLE for nonadherence to the Brazilian standardized cervical cancer screening program (N = 102).

	n (%)
Difficulty accessing a gynecologist	34 (33.3)
Lack of medical guidance	21 (20.6)
Health problems	14 (13.7)
Lack of time	12 (11.8)
No specific reason	21 (20.6)

SLE: systemic lupus erythematosus.

the study by Chung et al[1]; however, the second one reinforces the important role of the rheumatologist as an organizer in this matter.

The authors suggested in their article that a lack of a control group should be interpreted as a limitation of their study[1]; however, it does not diminish the study's credibility because patients with SLE present much higher risk of premalignant lesions than women without SLE.[3] The possibility of generalizability of the results found by Chung et al[1] may be reinforced by a previous study conducted in our same university hospital with 177 patients with SLE and 244 healthy controls, in which the mean interval from the last CCS for patients with SLE and controls was not different ($P > 0.05$), and only half of them were CCS guideline-congruent (E.M. Klumb, MD, PhD, unpublished data, 2010). In addition, Wadstrom et al and Tani et al showed similar rates of CCS in women with SLE compared with controls.[4,5]

Regarding the incidence of cervical cancer, we would like to emphasize that it is the fourth cause of cancer among women, mainly in high-income countries; however, it remains the second most frequent cancer among women in low- and middle-income countries.[6,7] The incidence of cervical cancer in countries with a low Human Development Index (HDI) is 3 times higher than that of high-HDI countries, and mortality rates are 6 times higher than those in countries with high HDI.[8] Further, a major effect on mortality was observed, particularly in the United States, where the cervical cancer death rate is 2-fold higher among women residing in high- vs low-poverty areas.[6]

The results presented by Chung et al,[1] in accordance with those of other authors, including ours, demonstrate the current alarming inadequacy of CCS in patients with SLE. In this context, it is important to emphasize that cervical cancer is silent until the late stages, and its control depends on adequate cervical cytology screening.[9] The adequacy of CCS is even more relevant among patients who are immunosuppressed who have higher frequency of human papillomavirus infection, a necessary condition for cervical cancer.[10] The data provided by Chung et al[1] and other authors emphasize the need for mandatory inclusion of CCS during regular consultations with women with SLE by rheumatologists, general practitioners, and gynecologists.

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The authors declare no conflicts of interest relevant to this article.

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