ORIGINAL ARTICLE

# Evaluation of vasomotor reactivity in systemic lupus erythematosus patients and its comparison with the control group

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**Background:** Neuropsychiatric abnormalities are among the most common manifestations of systemic lupus erythematosus (SLE). They have been proposed to be associated with impaired cerebral blood flow (CBF). Cerebral vasomotor reactivity (VMR) is a hemodynamic parameter effective in the autoregulation of CBF. The aim of the present study is to determine and compare the VMR of women with stable SLE and normal women. **Materials and Methods:** According to the study criteria 60 women in each group entered the study. VMR was evaluated with Transcranial Doppler (TCD) at rest and after one minute of breath holding. **Results:** There was no significant difference in the mean of age between two groups (31.76 ± 7.50 years in the SLE group versus 32.43 ± 4.55 years in the control group, *P* value: 0.64). The mean duration of SLE in the case group was 5.40 ± 3.60 years. The means of the Breath-Holding Index (BHI) in the SLE and control groups were 0.842 ± 0.72% and 0.815 ± 0.26%, respectively, which was not significantly different (*P* value: 0.82). **Conclusion:** This study indicates that the VMR of women with stable SLE is not significantly different from the age- and sex-matched normal population. However, further investigations on patients with longer SLE duration and more neuropsychological abnormality rates are suggested.

**Key words:** Cerebral blood flow, systemic lupus erythematosus, transcranial Doppler, vasomotor reactivity

## INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune and multisystem disease.[1] The central nervous system is often involved in patients with SLE,[2] and therefore, neuropsychiatric abnormalities are among the most common manifestations found in these patients.[3,4]

Although various investigations including serological tests, cerebrospinal fluid analysis, electroencephalogram, and different neuroimaging techniques have been widely used to perform neurolo gical assessments in SLE patients,[1,5] it is still difficult to detect and manage the neurological abnormalities of these groups due to lack of useful diagnostic methods.[6]

In addition, it has been reported that SLE patients may suffer from regional or general abnormal cortical blood flow[7] even in the absence of neurological symptoms.[6] Cerebral blood flow (CBF) is regulated by changes in the arteriole resistance, which leads to arteriole dilation and constriction.[8,9]

Given the importance of CBF, several imaging methods including positron emission tomography (PET), single-photon emission computed tomography (SPECT), and stable xenon-enhanced computed tomography have been employed to assess the compensatory response of cerebral autoregulation. However, all these methods are expensive and time-consuming.[10-14]

Therefore, since 1982, neurologists have been utilizing the transcranial Doppler (TCD) as a safe, noninvasive, and low-cost technique, to study large intracranial vessels at the base of the skull, and to evaluate the cerebral blood flow.[9,15,16] This method provides an assessment of different hemodynamic parameters such as flow velocity of intracranial arteries and cerebral vasomotor reactivity (VMR).[17]

Vasomotor reactivity is a hemodynamic parameter that represents the ability of the cerebral arterioles to dilate and constrict in response to specific stimuli. VMR is an important autoregulation mechanism that maintains cerebral blood flow.[18]

In patients with neurological involvements, TCD and VMR can provide easy and noninvasive assessment of the cerebrovascular system. This method can be helpful in the early diagnosis of some neurological abnormalities.[9,19]

In the light of the above, this study was designed to evaluate the VMR of the cerebral arteries of SLE patients and compare it with that of normal subjects.

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## MATERIALS AND METHODS

After approval of the study by the Ethics Committee of the Isfahan University of Medical Sciences and after obtaining informed consent, this comparative cross-sectional study was performed in the Neurology Outpatient Clinic of Al-Zahra Hospital, Isfahan, Iran, between March 2011 and April 2012.

On the basis of the reported influence of sex on VMR[20] and a higher prevalence of SLE among women, this study included only women.

Using the convenience sampling method, 60 stable female patients of age more than 18 years, with a diagnosis of SLE (according to the American college of rheumatology criteria), who were referred to the Neurology Outpatient Clinic, entered the case group. The controls were 60 age-matched, healthy women selected from the hospital staff. The exclusion criteria were diabetes mellitus, hypertension, head injury, cerebrovascular disease (transient ischemic attack, stroke, carotid artery stenosis more than 30%, and intracranial stenosis demonstrated by cervical Doppler sonography and TCD), chronic obstructive lung disease, hematological disease, and cancer.

In addition, non-cooperative subjects and those treated with hormonal medications, beta-blocking agents, calcium channel blockers, nitrates, vasodilatory drugs, and anticoagulants were excluded.

All subjects were asked to stop taking medications and smoking at least 12 hours prior to the TCD. A single neurologist who was unaware of the patients' group performed TCD while the subjects were in the supine position with their eyes closed. All investigations were performed in the morning, using a dual 2-MHz transducer, fitted on a headband. The trans-temporal window was used to insonate the middle cerebral artery (MCA).

In the present study, VMR was calculated by measuring the changes in the mean flow velocity (MFV) of the MCA induced by breath-holding.

After a five-minute period of normal room air breathing, the rest MFV was recorded. Next, the breath-holding MFV was recorded, after holding the breath for one minute.

The Breath holding index (BHI) was calculated from the following equation:

$$BHI(\%) = \frac{MFV_{Apnea} - MFV_{Rest}}{MFV_{Rest} \times 30} \times 100$$

The average of the bilateral BHI was considered as the subject BHI.

Data were analyzed by SPSS 16, using the independent *t*-test. *P* values less than 0.05 were considered statistically significant.

## RESULTS

At the end of the study, the data of two groups were analyzed.

There was no significant difference in the mean of the age between the two groups (31.76 ± 7.50 years in the SLE group vs. 32.43 ± 4.55 years in the control group, *P* value: 0.64). The mean duration of SLE in the case group was 5.40 ± 3.60 years (minimum one year, maximum 16 years).

Within the SLE group, 12 (20%) patients had nephritis, 32 (53%) patients had cutaneous manifestations, 34 (57%) patients had arthritis, four (7%) patients had seizure, two (3%) patients had cerebral vasculitis, and seven (12%) patients had thrombotic events. However, there was no significant difference in the BHI of patients with or without the aforementioned symptoms [Table 1].

## DISCUSSION

Systemic lupus erythematosus is an inflammatory disease that targets the vascular system and causes various vascular manifestations, such as, vasculitis, vasculopathy, vasospasm, thromboembolism, and premature atherosclerotic vascular disease.[21,22]

**Table 1: Comparison of BHI between patients with or without SLE symptoms**

| Current presentation | BHI (%) | *P* value |
|---|---|---|
| Nephritis | | |
| Positive (*N*:12) | 1.09±0.50 | 0.50 |
| Negative (*N*:48) | 0.85±0.87 | |
| Cutaneous symptoms | | |
| Positive (*N*:32) | 0.81±0.86 | 0.19 |
| Negative (*N*:28) | 1.25±0.47 | |
| Arthritis | | |
| Positive (*N*:34) | 1.00±0.88 | 0.52 |
| Negative (*N*:26) | 0.78±0.44 | |
| Neurological symptoms (seizure or cerebral vasculitis) | | |
| Positive (*N*:6) | 0.93±0.45 | 0.97 |
| Negative (*N*:54) | 0.94±0.82 | |
| Thrombotic events | | |
| Positive (*N*:7) | 0.99±0.41 | 0.90 |
| Negative (*N*:53) | 0.93±0.84 | |

Data are presented as mean±SD, *N*=Number of patients; BHI=Breath holding index, Comparison of BHI between the two groups demonstrated that the mean of BHI in the control group was 0.815±0.26%, which was not significantly different from the BHI of the SLE group (0.842±0.72%, *P* value: 0.82), SLE= systemic lupus erythematosus

Systemic lupus erythematosus patients may suffer from various primary and secondary conditions that can affect the vascular system and increase the risk of cerebrovascular problems. The primary causes include vasculitis, specific anti-neuronal antibodies, and lupus anticoagulant; while renal disorders, hypertension, and steroid administration have been suggested as secondary causes.[23]

Impairment of the vascular system may lead to disturbance in the CBF and cause neuropsychiatric abnormalities, which are common in SLE patients. Neuropsychiatric abnormalities are considered to be associated with either increased or decreased global and regional cerebral blood flow.[24-27]

Cerebrovascular reactivity is considered to be an important hemodynamic parameter that represents adaptation potentialities of the cerebral circulation system, ability of the cerebral arteries to respond to changing conditions of functioning, and to optimize CBF in compliance with them.[9,28]

It has been reported that vascular risk factors can impair VMR, and consequently, increase the risk of cerebrovascular events.[29] Therefore, evaluation of VMR and VMR changes in clinical conditions that affect the vascular system can be helpful.

To the best of our knowledge, this is the first study that has investigated the VMR of patients with SLE, and compared it with the normal population. We have studied women with stable SLE, compared them to an age-matched population of normal women, and found no significant difference between the two groups with regard to the average BHI of the MCA.

The value we have found for the BHI of the normal population is similar to the BHI reported by Mousavi *et al*. for this sex and age group.[20] However, there is no previous study that reports the BHI of the MCA for SLE patients.

Given the numerous factors that are considered to have adverse effects on the vascular system of SLE patients, the question is why we have not found a significant difference in BHI between SLE patients and the normal population.

Vasomotor reactivity is an index that demonstrates the cerebral reserve. It is associated with the difference between the minimum and maximum diameter of the cerebral arteries, and depends on many factors, such as, age, gender, systemic hypertension, atherosclerosis, and other vascular diseases that affect the elasticity of the vessels.[9,30-32] We have matched two groups with regard to sex and age, and selected stable patients according to the study criteria. Therefore, our findings mostly demonstrate the effects of SLE on VMR. A previous study by Roman and colleagues has demonstrated that vascular changes in SLE patients are time-dependent, and are significantly associated with the duration of the disease and duration of corticosteroid use.[33] They have shown that SLE patients with atherosclerotic plaques have average disease duration of 173 months, while it is 129 months in patients without atherosclerotic plaques.[33] The average disease duration of our SLE group was about five years (60 months), which is significantly lower than the proposed time required for atherosclerotic changes. Therefore, it is not surprising that we did not find significant changes in the VMR of these patients. Shorter disease duration is correlated with shorter duration of taking corticosteroids, which is another important factor that affects the vascular system. Another factor contributing to this result is that we included stable SLE patients, who had a low prevalence of neuropsychological abnormalities, and hence, they were not suffering from significant cerebrovascular problems.

A major limitation of this study was the inability of some subjects to hold their breath for one minute, which led to exclusion of participants or a need for repetitive investigations. This problem could be solved by employing other techniques for stimulating hypercapnia such as using acetazolamide.

## CONCLUSION

This study indicated that VMR of women with stable SLE was not significantly different from the age- and sex-matched normal population.

However, we suggest further investigations on SLE patients with longer disease duration, comparison of the VMR of patients with different SLE durations with the normal population, and comparison of the VMR of SLE patients with and without neuropsychological involvement, to provide a more reliable evaluation of the effects of SLE on the VMR of cerebral arteries.

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