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# Headache and systemic lupus erythematosus: is there an entity of "lupus headache"?

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*Abstract*

Headaches especially migraine has long been thought to be more prevalent in systemic lupus erythematosus (SLE) and are believed to be part of the SLE disease process. We sought to evaluate this by studying prospectively 50 SLE inpatients without known secondary causes for headache, using a standard questionnaire on headache. We used the IHS criteria for the classification of headaches. Our patients were compared with two sets of controls - 50 non-SLE hospital inpatients with no known disease that can cause headache and 208 normal community-based controls. We found that the prevalence of headache in SLE patients did not differ significantly from the controls (78% versus 82% (hospital controls) and 79.3% (community controls)). There was no significant difference in the prevalence of the various headache subtypes i.e. migraine, tension-type headache and other headaches among the three study groups. There was a significantly greater number of manifestations of stress in SLE patients with headache compared to those without headache. Relationship of headache to illness onset did not differ significantly between SLE patients and hospital controls. This study does not support the entity of 'lupus headache'. Headache in SLE patients appear more likely due to stress.

*Keywords:* headache, migraine, tension-type headache, systemic lupus erythematosus

## INTRODUCTION

Nervous system manifestations in systemic lupus erythematosus (SLE) are heterogeneous and reflect varied underlying pathophysiological mechanisms. Headaches are a common complaint in patients with SLE and may indicate varied underlying central nervous system abnormalities from cerebrovascular diseases (e.g. strokes, cerebral venous thrombosis, intracranial aneurysms), central nervous system infections to idiopathic intracranial hypertension [1]. Recurrent or chronic headache have also been described with increased frequency in SLE and have previously been found in 28% to 68% of SLE patients [2-9]. Although both migrainous as well as non-migrainous headaches are reported to be more common, it is migraine headaches that have been emphasised in most reports. A direct association between migrainous-type headaches and SLE involvement of the nervous system have been suggested [4, 5-10], the severity being correlated with disease activity and improvement seen with SLE therapy [7, 9].

Headache is an extremely common symptom, however and a coincidental association has to be excluded. Furthermore the classification of headaches used in previous studies were not uniform and none used the now widely accepted International Headache Society (IHS) criteria for classification of headaches [11].

Systemic lupus erythematosus is a common disease in Malaysia and was estimated to be 43/100 000 population [12]. In this study we aim to prospectively analyse the frequency and pattern of headache in our SLE patients compared to controls and thereby determine whether there exists an entity as a 'lupus headache'.

## MATERIALS AND METHODS

This study was carried out using a structured in-person interview with a standard questionnaire (Fig. 1). The SLE patients studied were admitted the University Hospital, University of Malaya, Kuala Lumpur and fulfilled the 1982 American College of Rheumatology (ACR) criteria for SLE [13]. They had no secondary causes for headache. Two control groups were selected. They were age and sex-matched non-SLE hospital inpatient controls with no history of central nervous system disease and no obvious

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1. **Race, age, sex and family income**
2. **How many headaches have you had during your life?** (0; 1-4; 5-9; more than 10)
3. **How many days during the last 12 months have you suffered from headache?** (0 days; 1-7 days; 8-14 days; 15-30 days; 31-180; more than 180 days)
4. **How long does your headache last if you do not take medication or if medication does not work?** (less than 30 minutes, 30 minutes to 4 hours, 4 to 24 hours, 24 to 72 hours, 3 to 7 days, more than 7 days)
5. **Location of headache** (right side, left side, alternating right and left side, alternating unilateral-bilateral, always bilateral, varies a lot, frontal, back of head, whole head, other)
6. **Type of pain** (pulsating, pressing/tightening, stabbing, other)
7. **Severity of pain** (mild, daily activities not inhibited, moderate, severe, daily activities suspended)
8. **Does your headache get worse with activities, climbing or walking down stairs?** (yes, no)
9. **Is your headache accompanied by nausea, vomiting, loss of appetite, photophobia, phonophobia, neurological symptoms?** (yes, no)
10. **What brings on your headache?**
11. **What do you do to relieve your headache?**
12. **What is the relationship of the headache to the onset of your illness?** (no headache, same, less headache, more headache)
13. **Evidence of stress** (poor appetite, poor sleep, feeling anxious/worried, feeling depressed)

FIG 1: Headache Questionnaire

cause for headaches and age and sex-matched community-based controls selected from subjects in a previously reported door to door community-based survey on headache prevalence in Malaysia [14]. We used the International Headache Study (IHS) criteria which is hierarchically constructed diagnostic classification for headache disorders to determine the headache subtypes in our study groups. The classification for migraine and tension-type headache appears to be more specific than in previously reported definitions.

We attempted to evaluate the presence of stress (from having an active illness and being in hospital) as a major factor in provoking headaches in our subjects as it was found to be a common precipitating factor of migraine and tension-type headache in our previous study of headache prevalence in Malaysia [14]. As stress is non-specific and difficult to define, we asked about four common symptoms viz. poor appetite, poor sleep, feeling anxious/worried and being depressed as manifestations of being under stress. We felt that the patients' perception of being stressed especially when having an illness may be important in precipitating headache. It is to control for this that we included a group of hospitalised but non-SLE inpatients.

Our subjects were also asked about the relationship of the severity of headache with the onset of illness to determine if headache severity correlated with the onset of other manifestations of their illness.

Statistical analysis of the differences in the various groups was carried out using the chi-square test.

## RESULTS

A total of 50 SLE patients were studied of which 7 patients had clinical central nervous system involvement. All SLE patients were defined as having active disease according to the Lupus Activity Criteria Count (LACC) [15]. Another 50 inpatients with illnesses other than SLE were interviewed as hospital controls. There were 208 subjects in the community-based control population group. The sex ratio for the SLE patients were 49 females to 1 male while all the hospital control patients and community controls were female. Their ages ranged from 9 to 64 years (mean 30.0 years) for SLE patients, 12 to 63 years (mean 33.2 years) for hospital controls and 16 to 45 years (mean 32.1 years) for community controls. The age distribution of the three study groups are shown in figure 2. The racial distribution is shown in figure 3.

The overall prevalence of headache for the previous year was 78% for SLE inpatients, 82% in hospital controls and 79.3% in the community control population. There was no significant differences between the SLE group and the two control populations ($\chi^2 = 0.04$; $p = 0.84$ for SLE patients versus community controls, $\chi^2 = 0.25$; $p = 0.62$ for SLE patients versus hospital controls).

The frequency and pattern of various headache disorders in SLE patients were as follows - migraine in 8 (16%) patients, tension-type headache in 15 (30%), other type of headaches in 16 (32%) of patients and no headaches in 11 (22%) patients. Of the hospital controls, 10 (20%) had migraine, 16 (32%) had tension-type

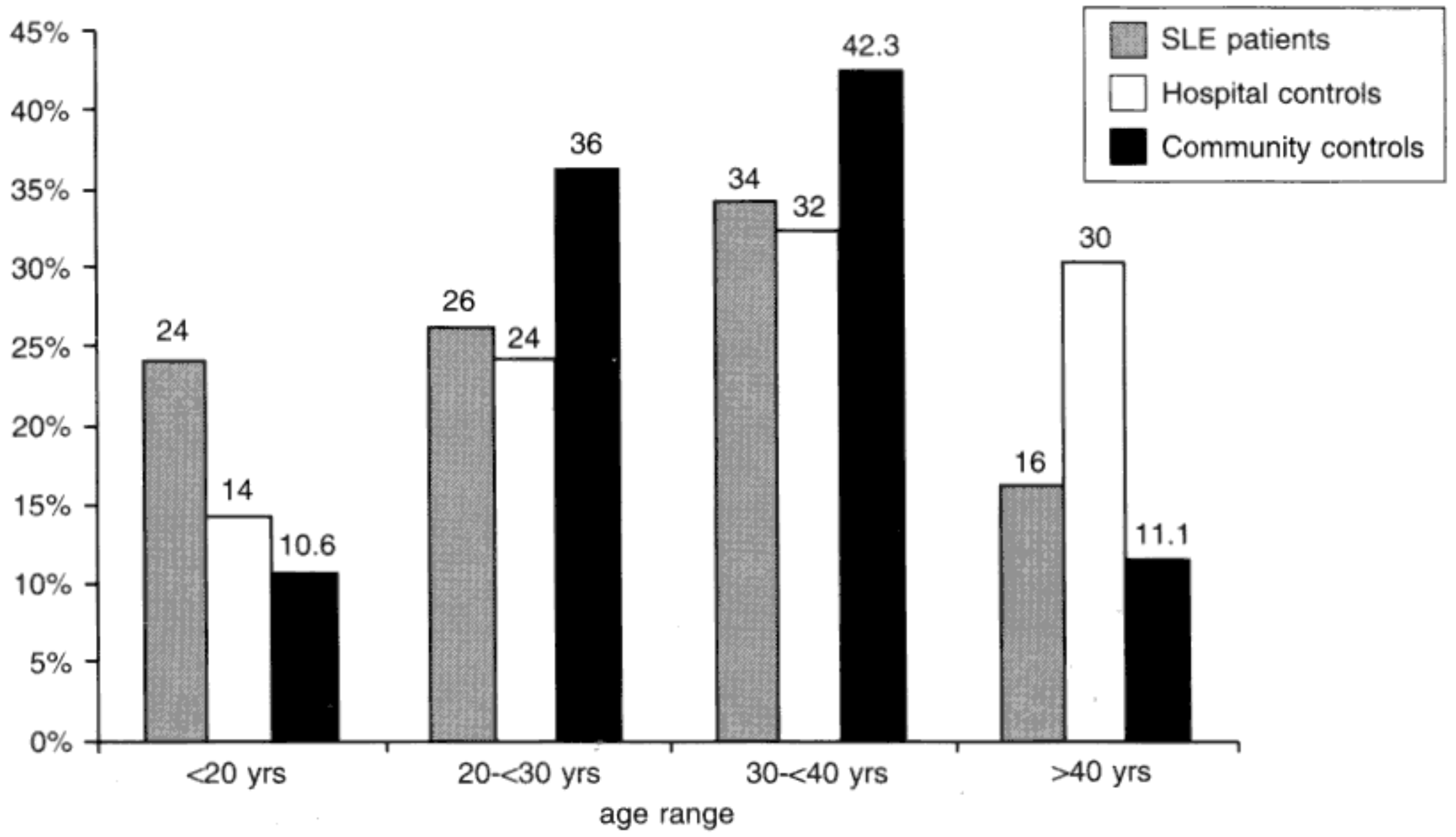


FIG 2: Age distribution for SLE patients, hospital controls and community controls

headache, 15 (30%) had other types of headache and 9 (18%) had no headaches. Among the community-based controls, 30 (14.4%) had migraine, 74 (35.6%) had tension-type headaches, 61 (29.3%) had other headaches and 43 (20.7%) had no headaches. Comparison of the headache prevalence by subtype between the various study groups are summarised in figure 4. There was no significant differences between SLE patients and the control groups with regards to the prevalence of migraine headaches nor between the two control groups themselves ($\chi^2 = 0.08$; $p = 0.78$ for SLE versus community controls and $\chi^2 = 0.27$; $p = 0.60$ for SLE patients versus hospital controls and $\chi^2 = 0.96$, $p = 0.32$ for hospital versus community

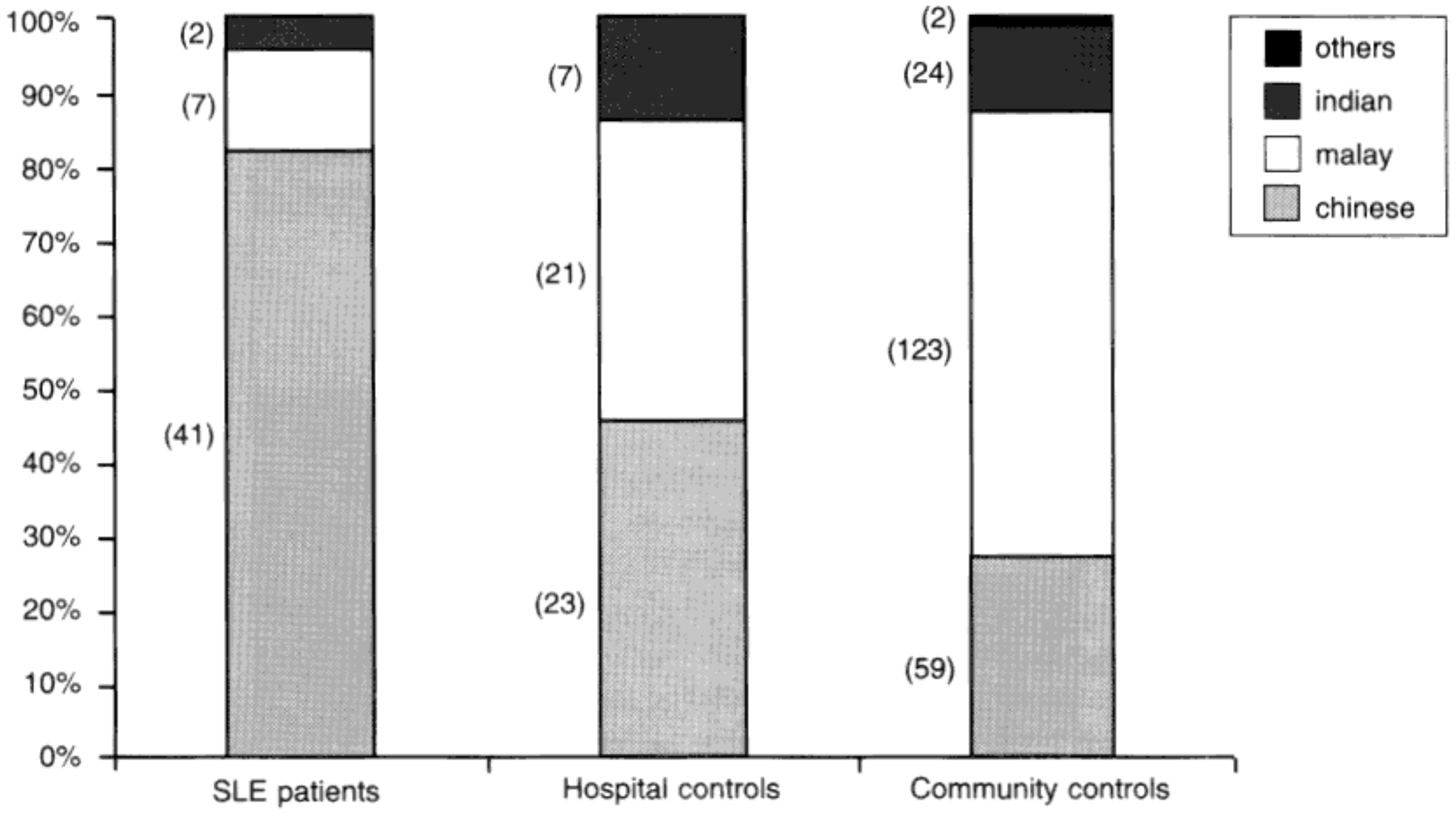


FIG 3: Racial distribution among SLE patients, hospital controls and community controls

( ) indicates the absolute number of patients

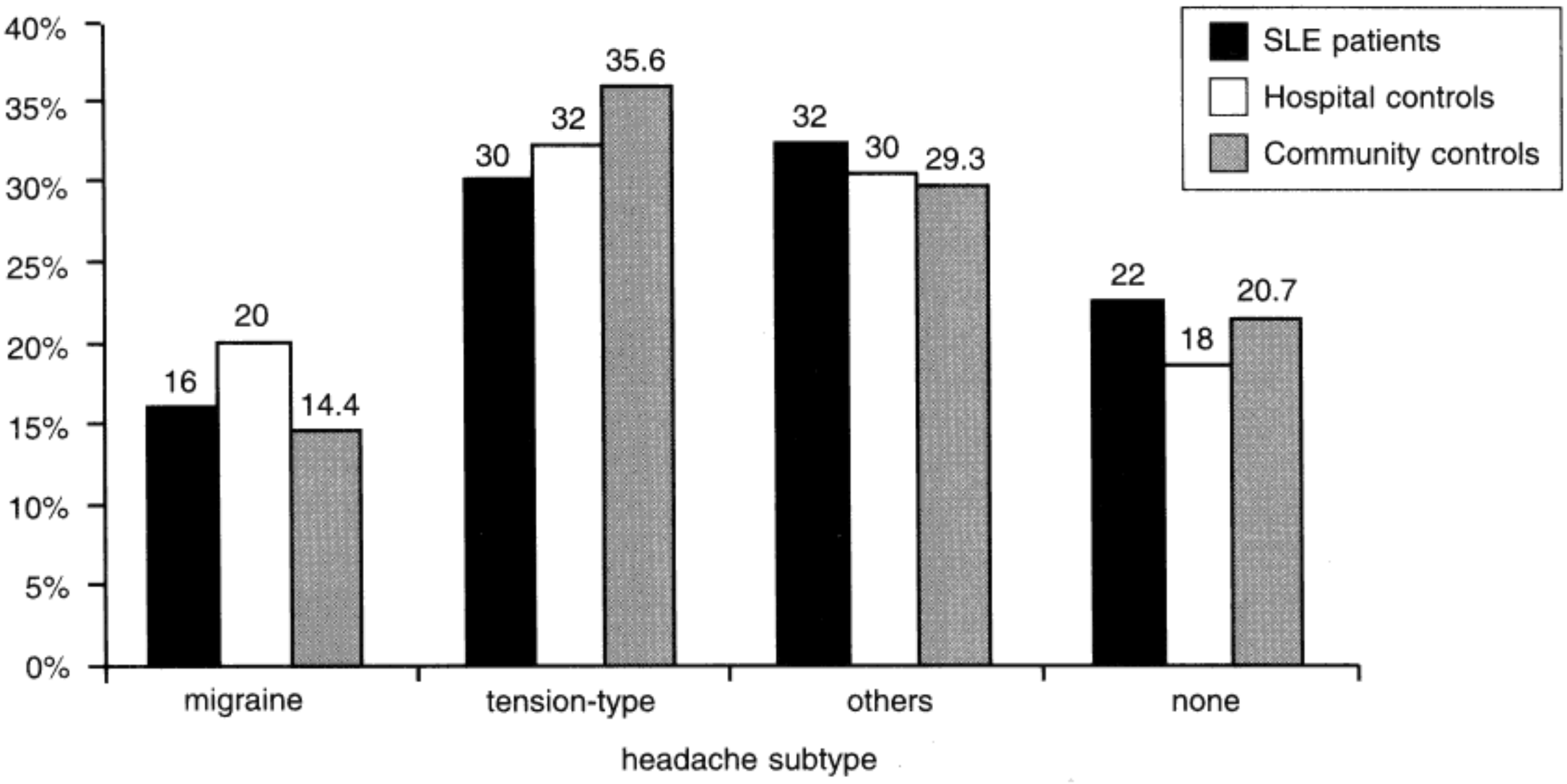


FIG 4: Comparison of headache prevalence by subtype between the study groups

controls). Similarly, prevalence of tension-type and other types of headache were not significantly different in the three groups.

29 (74.4%) of the 39 SLE patients with headache had one or more symptoms of stress compared to 5 (45.5%) of the 11 SLE patients without headache (Fisher's exact test p = 0.08). In order to be more certain of the evidence of stress, we considered the presence of at least two or more symptoms, and found that this significantly differed between the two subgroups (59% (23 of 29) of SLE 'headache' patients to 18.2% (2 of 11) of SLE 'non-headache' patients, $\alpha^2 = 5.71$, p = 0.017). Figure 5 summarises the frequency of stress symptoms between the groups.

We also asked our SLE patients about the relationship of the headache to the onset of their illness. Eight (20.5%) patients felt that they developed headaches or had more frequent headaches after the onset of their illness, 5 (12.8%) had less and 26 (66.7%) had no change in their headache frequency. Among hospital control patients with headache, 5 (12.2%) had more headaches, 4 (9.8%) had fewer headaches while 32 (78%) felt there was no change in their

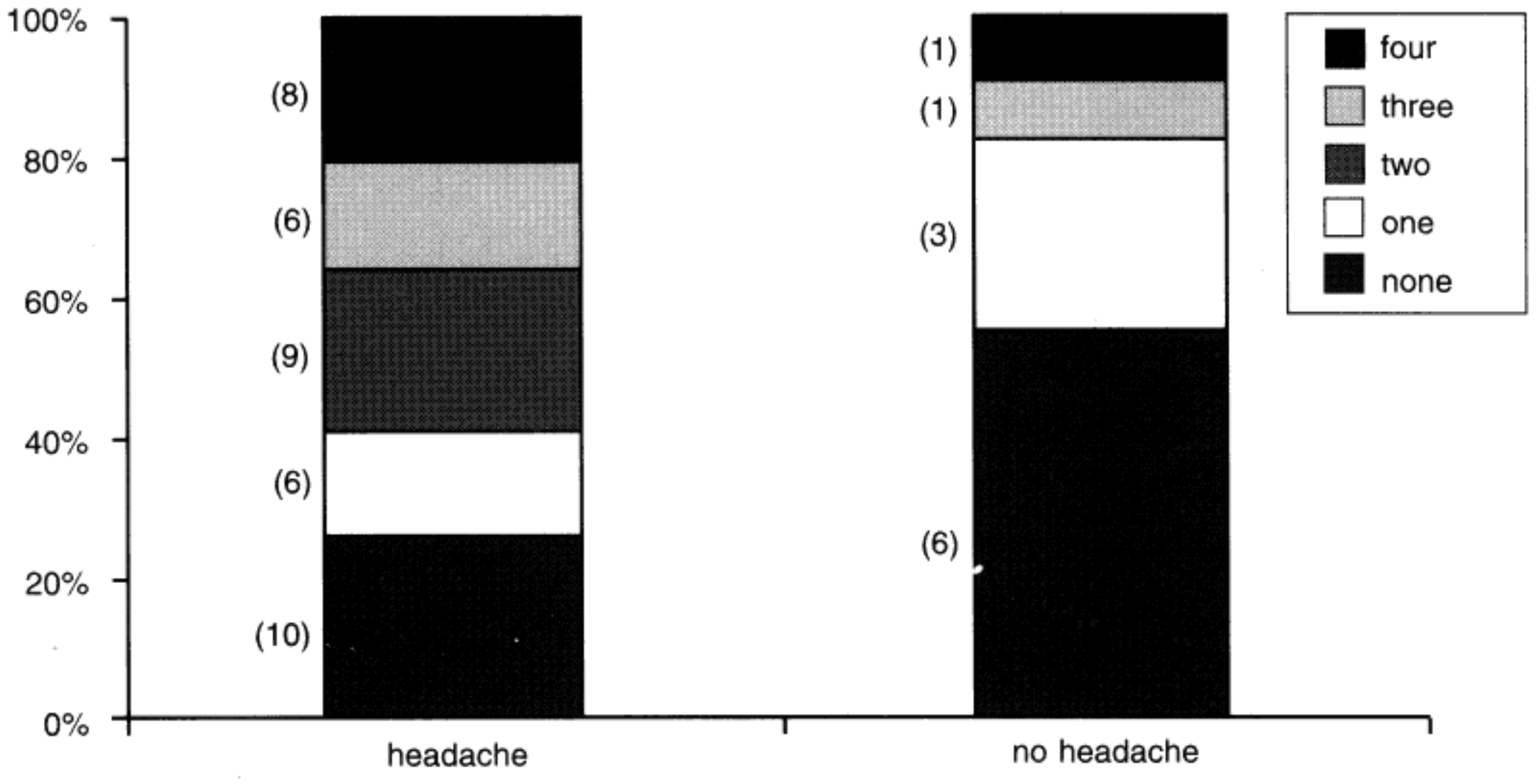


FIG 5: Comparison of the number of symptoms of stress between SLE patients with and without headache

( ) indicates the absolute number of patients

headache frequency, after onset of their illness. There was no statistically significant differences between the two groups of patients in this aspect.

## DISCUSSION

Central nervous system involvement in SLE is common and headache has long been described as a feature in SLE [2-9]. The 'lupus headache' has been described as migrainous in nature and temporally related to the onset of SLE [6, 7, 9]. The headache was said to be related to disease activity in one study [9] but not in others [4, 7]. A relationship to antiphospholipid antibodies was postulated [14] but has not been confirmed subsequently [8, 9]. Most previously reported series of patients were either retrospective or prospective but did not include a control group. Only one recent study included a normal control group consisting of patients' relatives or hospital staff [9]. This does not however take into account of the stress of being ill and/or being hospitalised which may be an important precipitants of headache. Headache is an extremely common symptom, the patient's subjective perception of his/her circumstances may lead to development of headache unrelated to the underlying disease. Therefore we chose to include and additional control group of non-SLE hospital inpatients.

The prevalence of headache subtypes in any case series would depend upon the chosen definition of the headache disorder. The definition of migraine used in previous studies have been variable and we are the first to utilise the IHS criteria which have been specifically designed for the use of headache research. Comparison between studies would be greatly facilitated with the routine use of these criteria.

Our study demonstrates that the overall prevalence of headache among SLE patients is not significantly different from hospital inpatient or community-based controls. Migraine was not significantly more prevalent among SLE patients compared to the control groups. This was also true for tension-type and other types of headaches. Comparing SLE patients with and without headache, evidence of stress was more common among those with headache. Significantly more SLE 'headache' patients had at least two or more symptoms of stress compared to SLE non-headache patients. This suggests that stress may play an important role in the aetiology of headache.

There did not appear to be any significant difference in the relationship of headaches to the onset of illness between the SLE patients and the hospital inpatient control group. Again, this would not seem to support the specific nature of an SLE headache.

This study does not support the entity of a 'lupus headache' as a common cause of headaches in patients with SLE. While it appears unlikely that headache in the majority patients is due to the disease process itself, the study does not exclude the possibility of this occurring in the individual patient with headache. To prove this, we would then have to study exclusively neuropsychiatric lupus patients as compared to controls - such a study has yet to be carried out.

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