

## ORIGINAL ARTICLE

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## Factors correlated with emotional instability in SLE outpatients

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**Abstract** Eighty-four female outpatients with systemic lupus erythematosus (SLE) who are able to live on their own were investigated. We statistically analyzed the relationship between emotional instability based on psychological tests (Cornell Medical Index), and physical, medical, and social factors based on both our clinical records and original questionnaires. The emotional instability was related to not “working,” an older “age at the time of SLE diagnosis,” being “anxious about the adverse effects of steroids,” or not “understanding the details of the disease and treatment at the time SLE treatment was started.” No relationship with previously experienced physical factors was observed. In addition, no relationship with disease activity was observed either. We identified the characteristic correlation between emotional instability and medical and social factors in this study. Paying close attention to these factors may thus be useful in both preventing the appearance of psychological problems and developing effective early treatment strategies.

**Key words** Systemic lupus erythematosus · Emotional instability · Social factors · Medical factors · Physical factors

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### Introduction

The cumulative survival rate of patients with systemic lupus erythematosus (SLE) over a period of 10 years has improved to 85%–93%,<sup>1,2</sup> and the long-term life prognosis has also markedly improved. In addition, there have been numerous reports on the diagnosis and treatment of central nervous system (CNS) lupus.<sup>3</sup> However, although it is known that patients with SLE can continue to lead an independent life while suffering from psychological agony,<sup>4</sup> few reports have been published describing the milder episodes of psychological distress of SLE outpatients. Only Shortall et al.<sup>4</sup> has investigated the milder episodes of psychological distress among outpatients with SLE, and thus showed a correlation between anxiety and social interactions. The aim of this study was to determine the concrete background factors (physical, medical, and social) related to emotional instability in female SLE outpatients leading an independent life. We examined emotional instability employing the Cornell Medical Index (CMI) Health Questionnaire,<sup>5,6</sup> which is widely used in Japan to estimate emotional state. We used multivariate statistical procedures (stepwise multiple logistic regression analysis) to analyze of the correlation between psychological features and background factors. The factors selected for this study are based on both the findings of previous studies,<sup>4,7–16</sup> and our own clinical experience and discussions with both rheumatologists and liaison psychiatrists. We have already published the study design on hemodialytic patients.<sup>17</sup> It appears essential to take timely and appropriate preventive and therapeutic measures, not only to treat SLE itself effectively, but also to prevent a variety of other psychotic disorders. The aim of our study is thus to help shed some light on this problem.

### Subjects

The investigation included female outpatients, aged 20 years or older ( $n = 120$ ), who visited the Collagenosis Clinic

at the First Department of Internal Medicine, Faculty of Medicine, Kyushu University, from November 1996 to March 1998, and whose symptoms conformed with the revised criteria of the American Rheumatism Association for SLE.<sup>18</sup> Our hospital is a general hospital of regional hub status, which has 1300 beds. In this study, any patients who also had mixed connective tissue diseases and other collagenosis were excluded. Out of the 120 patients, all cases were able to respond to the psychological test, although 4 patients were excluded from testing after discussions between rheumatologists and liaison psychiatrists: one immediately after having lost a child in a traffic accident, one immediately after recovery from CNS lupus, one because of severe obsessive symptoms, and one who refused SLE treatment. In addition, 5 patients refused to take part in the investigation. Finally, 111 out of the 120 subjects gave their consent to join the present study, underwent the psychological test described below, and filled out the questionnaires specifically prepared for this study. Out of the 111 patients, 84 (75.7%) responded fully to the psychological test and the questionnaires without missing any items. The analysis was thus carried out on these 84 subjects.

## Methods

We evaluated emotional disturbance by using psychological testing the reliability and validity of which has been verified in Japan, and we also used a questionnaire designed by ourselves. The factors considered to affect emotional instability were classified into three groups, physical, medical, and social, and an analysis was also made to determine how these characteristics were affected by each factor. The background factors were set up based on discussions between rheumatologists and liaison psychiatrists, while taking into consideration any factors suspected to be clinically responsible for emotional instability, and also referring to other factors cited in the literature. After establishing the presence or absence of emotional instability as dependent variables, and physical, medical, and social factors as independent variables affecting emotional instability, the investigation was carried out using statistical methods to determine how physical, medical, and social factors affected the psychological characteristics of "yes" and "no" patient groups. We have already published<sup>17</sup> the study design for this investigation.

### Dependent variables

Regarding emotional instability, we used the CMI and assessed our findings by the Fukamachi criteria,<sup>6</sup> which are widely used in Japan. The CMI<sup>6</sup> includes significant comprehensive information about all the patient's medical problems. The CMI consists of 18 sections (195 questions) referring to physical and psychological symptoms. The sub-

jects were classified into four groups (areas I–IV) according to the distribution of total affirmative responses for C (cardiovascular system), I (fatigability), and J (frequency of illness), and the total affirmative responses for the psychological problems, namely M (inadequacy), N (depression), O (anxiety), P (sensitivity), Q (anger), and R (tension). The Fukamachi criteria define area I as "diagnosed to be normal (normal)," area II as "provisionally diagnosed to be normal (subnormal)," area III as "provisionally diagnosed to be neurotic (subneurotic)," and area IV as "diagnosed to be neurotic (neurotic)."

In the present study, we classified the patients who had emotional instability as either area III or area IV, and the patients who did not have emotional instability as either area I or area II, based on the CMI.

### Independent variables

After consideration of previous reports and discussions between rheumatologists and liaison psychiatrists, three groups were set up which related to the significant factors affecting the psychological characteristics mentioned above. These factor groups were determined based on clinical records and our original questionnaires, and included any (1) physical factors or physical symptoms which the patient had suffered from before the start of the present investigation, (2) medical factors, such as steroid use, disease activity, or other factors deemed to be directly related to the treatment, and (3) social factors, such as those which are closely related to the patient's particular background.

#### *Physical factors*

The physical symptoms of SLE patients at the time of the investigation have previously been reported to affect their psychological state.<sup>16</sup> SLE patients tend to suffer from various physical symptoms, including side effects due to steroid administration. It would be helpful in treating such patients if we could have a better understanding of how a physical symptom, once experienced, may continue to affect a patient mentally even after the symptom has disappeared. For this reason, we noted what kind of physical symptoms the patient had suffered from previously. In the questionnaire on physical factors, we asked: "What symptoms have you suffered from in the past?" and we allowed multiple answers. Regarding physical factors, three subgroups containing 13 items in total were set up, as shown in Table 1. The subgroups were: (a) factors affecting body image, including "changes in countenance," "gain in body weight," "hair loss," "facial erythema," "change in body form," and "increase in body hair," (b) factors giving physical pain, including "Raynaud's phenomenon," "arthralgia," "oral aphtha," "photosensitivity," "fever," and "visual loss," and (c) factors affecting body image and giving physical pain through claudication or hypokinesia, which contained one single item, "necrosis of the femoral head." In addition, three

**Table 1.** Correlation of background factors

|  |         | Emotional instability |                | P-vale          |
|--|---------|-----------------------|----------------|-----------------|
|  |         | -                     | +              |                 |
| <b>Physical factor</b>                     |         |                       |                |                 |
| (a) Factors affecting body image           |         |                       |                |                 |
| Change of countenance                      | Present | 25 (47.2%)            | 18 (58.1%)     | 0.3451          |
| Gain in body weight                        | Present | 22 (41.5%)            | 20 (64.5%)     | 0.0705          |
| Hair loss                                  | Present | 22 (41.5%)            | 14 (45.2%)     | 0.9220          |
| Facial erythema                            | Present | 25 (47.2%)            | 15 (48.4%)     | 1.0000          |
| Change of body form                        | Present | 11 (20.8%)            | 7 (22.6%)      | 1.0000          |
| Increment of body hair                     | Present | 12 (22.6%)            | 7 (22.6%)      | 1.0000          |
| Total (affecting body image) (0–6)         | Mean    | 2.2                   | 2.6            | 0.2211          |
| (b) Factors giving physical pain           |         |                       |                |                 |
| Raynaud's phenomenon                       | Present | 17 (32.1%)            | 13 (41.9%)     | 0.5002          |
| Arthralgia                                 | Present | 31 (58.5%)            | 15 (48.4%)     | 0.5025          |
| Oral aphtha                                | Present | 8 (15.1%)             | 11 (35.5%)     | 0.0594          |
| Photosensitivity                           | Present | 10 (18.9%)            | 11 (35.5%)     | 0.1510          |
| Fever                                      | Present | 21 (39.6%)            | 13 (41.9%)     | 1.0000          |
| Visual loss                                | Present | 11 (20.8%)            | 9 (29.0%)      | 0.5525          |
| Total (factors giving physical pain) (0–6) | Mean    | 1.8                   | 2.3            | 0.1841          |
| (c) Necrosis of femoral head               | Present | 6 (11.3%)             | 6 (19.4%)      | 0.4887          |
| (a) + (b) + (c) Total (0–13)               | Mean    | 4.2                   | 5.1            | 0.0712          |
| <b>Medical factors</b>                     |         |                       |                |                 |
| <i>Understanding of the disease</i>        | Present | 26 (49.1%)            | 5 (16.1%)      | <u>0.0054**</u> |
| Period of suffering from SLE (years)       | Mean    | 10.6                  | 11.6           | 0.6064          |
| Admission frequency (times)                | <2      | n = 36                | n = 16         |                 |
|  | 2,3,4   | n = 10                | n = 8          |                 |
|  | 4<      | n = 7                 | n = 7          | 0.3149          |
| Used steroids                              | Present | 48 (90.6%)            | 30 (96.8%)     | 1.0000          |
| Dosage of steroids (mg/day)                | Mean    | 7.8                   | 7.6            | 0.9888          |
| Anxious about adverse effects of steroids  | Present | 35 (66.0%)            | 27 (87.1%)     | 0.0627          |
| Disease activity                           | Present | 5 (9.4%)              | 5 (16.1%)      | 0.4874          |
| <b>Social factors</b>                      |         |                       |                |                 |
| Age at the time of diagnosis (years)       | Mean    | 29.9                  | 32.8           | 0.2243          |
| Age at the time of investigation (years)   | Mean    | 39.2                  | 43.6           | 0.2521          |
| <i>Spouse</i>                              | Present | 42 (79.2%)            | 16 (51.6%)     | <u>0.0164*</u>  |
| Solitary living                            | Present | 2 (3.8%)              | 3 (9.7%)       | 0.3531          |
| Living with children of age below 15       | Present | 16 (30.2%)            | 4 (12.9%)      | 0.1262          |
| Losing friends after suffering from SLE    | Present | 1 (1.9%)              | 4 (12.9%)      | 0.0595          |
| Smoking                                    | Present | 8 (15.1%)             | 5 (16.1%)      | 1.0000          |
| Higher education                           | Present | 28 (52.8%)            | 18 (58.1%)     | 0.8119          |
| Reduced satisfaction in sex life (n = 55)  | Present | 7 (18.4%)             | 3 (17.6%)      | 1.0000          |
| <i>Working</i>                             | Present | 51 (96.2%)            | 21 (67.7%)     | <u>0.0006**</u> |
| <b>Troubles</b>                            |         |                       |                |                 |
| Job  | Present | 7 (13.2%)             | 10 (32.3%)     | 0.0694          |
| Personal relationships in family           | Present | 8 (15.1%)             | 5 (16.1%)      | 1.0000          |
| <i>Income</i>                              | Present | 6 (11.3%)             | 11 (35.5%)     | <u>0.0174*</u>  |
| Marriage (n = 18) <sup>a</sup>             | Present | 5 (50.0%)             | 3 (37.5%)      | 0.6641          |
| Pregnancy (n = 18) <sup>a</sup>            | Present | 3 (30.0%)             | 3 (37.5%)      | 0.9999          |
| Pregnancy (n = 19) <sup>b</sup>            | Present | 9 (60.0%)             | 0 (0%) n = 0/4 | 0.0867          |

<sup>a</sup>Single women in their 20s and 30s

<sup>b</sup>Married women in their 20s and 30s

Understanding of the disease: (able to understand the details of at the disease and treatment at time of starting the SLE treatment)

\* $P < 0.05$ ; \*\* $P < 0.01$

other items were also included: the total score of (a) items, the total score of (b) items, and the “number of total items for uncomfortable physical complaints,” which was the total score for (a), (b), and (c). The investigation was carried out based on all 16 items.

In the case of arthralgia, its location was not specified, and the subject was requested to put a check mark wherever the symptom appeared in her body.

We initially focused our attention on the impact of existing physical symptoms. We discovered, however,

that asking about specific side effects directly and making the patient confront them again tended to induce unfavorable psychological effects. As a result, this question was finally omitted, and only existing physical symptoms were evaluated based on the disease activity in the medical factors group described below. For this reason, it was impossible in the present study to analyze how each existing physical symptom affected the psychological aspects.

### Medical factors

Seven medical factors were examined, as shown in Table 1. The questionnaire included two questions: "Did you understand the details of the disease and treatment at the time of starting SLE treatment?" (a yes answer to this question is described as "understands the disease and treatment . . ."), and "Are you anxious about the adverse effects of steroids regardless of whether or not you have experienced them before?" (a yes answer to this question is described as "anxious about the adverse effects of steroids . . ."). We checked the clinical records of all patients to determine whether or not they had previously been administered steroids. Two groups were set up depending on whether the patients answered yes or no to these three items. Another question was: "How many times have you been hospitalized for SLE treatment?", and the frequency was classified into three levels: 0–1, 2–4, and 5 times or more. Two additional items were the "period of suffering from SLE," which included the number of years from the diagnosis to the time of investigation, and the "dose of steroids (mg/day)." In addition, "disease activity" was examined by the lupus activity criteria count (LACC),<sup>19</sup> which meant setting up two groups recording the presence or absence of its activity. In the present study, LACC was partly modified in some of the activity assessing items: "LE cell positive" was replaced by "LE test positive," and "anti-DNA antibody positive" by "anti-double strand DNA positive (>10IU/ml)."

### Social factors

Sixteen social factors were examined, as shown in Table 1. After examining the clinical records, two items were set up, i.e., "age at the time of investigation" and "age at the time of diagnosis," while eight items were derived from the questionnaire, i.e., "spouse," "living with children below age 15," "smoking," "losing friends after suffering from SLE," "higher education," "solitary living," "working," and "reduced satisfaction in sex life (if married)". For each of these items, two groups were formed depending on yes or no answers to the questions. In addition, questions asking about subjective complaints were set up to collect information regarding troubles in their actual life. Five multiple choice items were presented: "personal relationships in family," "job," "income," "pregnancy," and "marriage," and two groups, were established depending on the yes or no answers for each item. These five questions were designed so that the patient would answer yes if she was worried about the item concerned, while not asking for any specifics. It is therefore possible that details of such worries may vary greatly among patients. For instance, the term family in the item "personal relationships in family" has a wide range of meaning: parents and children, brothers and sisters, or husband and wife. Similarly, other items also had a wide range of meaning.

The item "marriage" was applicable to single women in their 20s and 30s, and "pregnancy" to single and married

women in their 20s and 30s. "Job," including regular, part-time, and housewife, could be answered yes or no. "Higher education" applies to patients whose education lasted more than 12 years, that is, 9 years of obligatory education plus 3 years of high school education. It should be noted that in Japan the percentage of those graduating from high school education exceeds 90%.

### Procedures

At the time of consultation at the internal medicine clinic, a physician explained the purpose of the investigation to the patients and showed them a written document. Patients giving their informed consent were then examined. At the same time, an explanation was given regarding both CMI and our own questionnaires prepared for the present study, and thereafter various forms were also given to the patients to complete at home and later return by mail.

### Statistical analysis

Regarding the yes and no groups (independent variables) for emotional instability (dependent variables), the difference in the distribution of physical, medical, and social factors was analyzed by the  $\chi^2$  test (with Yeats' correction), Fischer's direct probability calculation, and the Mann-Whitney *U* test. The level of significance was set at 5%, below which an event was regarded as statistically significant. In addition, a stepwise multiple logistic regression analysis was used to evaluate the correlation of each of the psychological features (dependent variables) with the physical, medical, and social factors (independent variables). The BMDP program LR was used for the stepwise multiple logistic regression analyses, which were performed to evaluate the relationship between each psychological feature and the background factors (physical, medical, and social factors). Using this method, the most significant associated variable is thus entered into the model. After adjusting for each variable in turn, the most significant variable is then added to the model. This procedure continues until there are no more variables which meet the entry criterion ( $P < 0.05$ ). We are able to use many independent variables by using this analysis. All statistical analyses were performed using the BMDP Statistical Software on a SPARC Station 20.

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## Results

The mean age, mean period of suffering, disease activity, and daily dose of steroids

The mean age of all 84 subjects was 41.3 years (SD  $\pm$  12.1; maximum 68, minimum 20), their mean age at diagnosis was 31.0 years (SD  $\pm$  10.1; maximum 60, minimum 14), and the

mean suffering period was 10.9 years (SD  $\pm$  6.8; maximum 29, minimum 1). The disease activity was positive in 10 subjects and negative in 74. The mean daily dose of steroid medication was 7.7 mg (SD  $\pm$  4.5; maximum 20, minimum 0), based on conversion of the various medications into the same dosage for prednisolone.

### Emotional instability

Based on the Fukamachi criteria described above, 21.4% of subjects ( $n = 18$ ) were in area I, 41.7% ( $n = 35$ ) were in area II, 23.8% ( $n = 20$ ) were in area III, and 13.1% ( $n = 11$ ) were in area IV. Hence, 36.9% of the subjects were diagnosed as having emotional instability, or as having subemotional instability when they had previously been thought to have emotional instability.

Results of the  $\chi^2$  test (with Yeats' correction), Fischer's direct probability calculation, and the Mann-Whitney  $U$  test

A significant correlation was recognized between emotional instability and one of the medical factors, namely "understanding of the disease and treatment." Statistically significant relations were found between social factors "spouse," "working," and trouble with "income," but no correlation was seen with the physical factors (Table 1).

### Results of a stepwise multiple logistic regression analysis

Three factors, "sexual satisfaction," "pregnancy," and "marriage," were excluded because the total number of subjects was less than 84. For physical factors, we only analyzed the following four factors: total score for (a) items, total score for (b) items, single (c) item, and total score for (a) + (b) + (c) items. These were mentioned in the Methods section, and were examined using stepwise multiple logistic regression analysis. Table 2 shows the results of a stepwise multiple logistic regression analysis with the level of significance at below 5%.

Emotional instability was significantly affected by not "working" and an older "age at the time of SLE diagnosis" among the social factors, and by "Anxiety about the ad-

verse effects of steroids" and not really "understanding the disease and treatment" among the medical factors.

Twenty-seven patients whose answers were not returned

The mean age at the time of the investigation was 38.7 years (SD  $\pm$  12.0; maximum 61, minimum 20), the mean age at the time of diagnosis was 29.2 years (SD  $\pm$  10.8; maximum 56, minimum 16), the mean span of suffering from SLE was 9.9 years (SD  $\pm$  6.0; maximum 24, minimum 0), the disease activity was positive in three and negative in 24 subjects, and the mean daily steroid dose was 6.6 mg (SD  $\pm$  4.2; maximum 15, minimum 0), as converted into the same dosage used for prednisolone. There was no statistically significant difference between the 84 patients whose data were returned and the 27 patients whose data were not returned regarding their age at the time of the investigation, age at the time of diagnosis, period of suffering, disease activity, and daily dose of steroids. The age at the time of the investigation, age at the time of diagnosis, period of suffering from SLE, and daily dose of steroids were examined by the Mann-Whitney  $U$  test, and the disease activity was examined by Fischer's direct probability calculation.

## Discussion

### Emotional disturbance

According to previous reports,<sup>20-23</sup> where the CMI was applied to patients with collagenosis, including SLE, areas III + IV ranged from 43.8% to 77.8%. These discrepancies may be attributed to differences in the treatment conditions regarding in-patients alone,<sup>20,21</sup> in- plus out-patients,<sup>22</sup> and outpatients alone,<sup>23</sup> and the inclusion of other types of collagenosis disease.<sup>21,22</sup> According to Nagaoka et al.,<sup>23</sup> who investigated female outpatients with SLE alone, just as for 24 patients in the present study whose data were obtained, Areas III + IV was 45.8%, and these findings also correlated with our data. Despite the time span of about 15 years which separated these two studies, no appreciable differences were found, thus suggesting that these psychological problems remain unsolved in Japan.

**Table 2.** Results of stepwise multiple logistic regression analyses

|   | Coefficient | Coef./SE | Odds ratio | P-value |
|---|-------------|----------|------------|---------|
| Emotional instability                     |             |          |            |         |
| Working                                   | -2.463      | -2.69    | 0.0852     | 0.0018  |
| Anxious about adverse effects of steroids | 1.567       | 2.08     | 4.79       | 0.0218  |
| Understanding of the disease              | -1.333      | -2.11    | 0.264      | 0.0257  |
| Age at the time of SLE diagnosis          | 0.05342     | 1.96     | 1.05       | 0.0431  |
| Constant                                  | -0.9204     | -0.763   |            |         |

Understanding of the disease: (able to understand the details of the disease and treatment at the time of starting the SLE treatment)

When a stepwise multiple logistic regression analysis was performed, a correlation was recognized between emotional instability and “working” among the social factors. “Working” includes housework and part-time jobs, and is considered to have a social influence on emotional instability. A correlation with the “age at the time of diagnosis” was also seen. There has been no report on the relationship between the age at the time of diagnosis and psychological problems. As this age rises, the role of a person in society grows. It may be speculated that suffering from SLE at a greater age leads to the loss or restriction of this social role and thus has a significant mental impact on the patient, thereby inducing emotional instability. Among the medical factors, anxiety about the side effects of steroids was found to correlate with emotional instability. In the future, further study on how to reduce anxiety about steroid side effects and how to provide treatment to suppress the adverse effects of steroid medication is called for. Not understanding the disease or the treatment was also found to be related to emotional instability.

Emotional instability means psychological fragility to various stress agents. Those patients showing emotional disturbance have psychological problems such as depression, anxiety, and confusion more frequently than those who do not. Since it is highly probable that these psychological problems affect their physical treatment and their quality of life, we regard it as clinically important to identify patients with emotional instability as early as possible in order to take appropriate preventive measures.

We consider that a check list of psychological problems and screening using this list, as well as close cooperation between psychiatrists and rheumatologists, would be useful in overcoming the emotional problems of SLE patients.

#### Limitations of the study

The present study using established psychological tests has certain limitations. First, the questions in the psychological tests related to physical conditions may be affected by symptoms associated with SLE and steroid administration. In the future, specific tests used exclusively for SLE patients should be developed so that SLE patients may receive a more accurate psychological evaluation. Second, since this was a cross-sectional study, the progress of psychological symptoms could not be followed. It is therefore necessary to design a prospective study including the treatment effect of evaluating psychological problems in detail. Third, we did not examine background factors specific to the SLE outpatients in this study, but only factors of practical importance for the treatment of all female SLE outpatients. A comparison with other chronic diseases may thus be needed to determine the specificity for SLE. In addition, a qualitative analysis based on detailed interviews to obtain sufficient data regarding each patient’s life history and disease history may be useful for finding specificity. Owing to these limitations, adequate care should be taken about incorporating our results into the development of various treatment regimens for SLE patients in general.

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