

## Prevalence of Chronic Fatigue Syndrome in a Community Population in Japan

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*The Department of Public Health, Gifu University School of Medicine, Gifu 500-8705, <sup>1</sup>Center for Research in Behavioral Medicine and Health Psychology, University of South Florida, FL, USA, <sup>2</sup>Yamazumi Hospital, Kofu 400-0007, and <sup>3</sup>Department of Sociocultural Environmental Research, National Institute of Mental Health, Ichikawa 272-0827*

KAWAKAMI, N., IWATA, N., FUJIHARA, S. and KITAMURA, T. *Prevalence of Chronic Fatigue Syndrome in a Community Population in Japan.* Tohoku J. Exp. Med., 1998, 186 (1), 33-41 — In order to know the prevalence of chronic fatigue syndrome (CFS) in a community population in Japan, we analyzed data from a population-based interview survey. Two cases out of 137 respondents experienced chronic fatigue during a period of nine months, suffered from 50% or more reduction of daily activity due to fatigue and had no other physical or psychiatric diagnosis. Both of the two cases fulfilled the 1994 Centers for Disease Control (CDC) criteria and the British criteria. The point and nine-month prevalence rates of CFS were both 1.5% (95% confidence intervals, 0.4-5.2%). None fulfilled the 1989 CDC criteria for CFS. The prevalence rate of CFS was higher than those in previous studies in the Western countries, suggesting a need for future research on cross-cultural differences in the definition, prevalence and symptomatology of CFS. ——— chronic fatigue syndrome; prevalence; community survey; Japan © 1998 Tohoku University Medical Press

Chronic fatigue syndrome (CFS) is an illness that has a large public health implication, with unknown etiology. Establishing the prevalence of the disorder is important for planning a health care service for the disorder, as well as for clarifying the nature of the disorder. A wide range of the prevalence of CFS has been reported in community populations. The point prevalence was 37 per 100 000 in an Australian population based on the information from physicians in the community (Lloyd et al. 1990). Price et al. (1992) employed an approximate

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diagnosis to the 1988 US Centers for Disease Control (CDC) criteria (Holmes et al. 1988) using the Epidemiologic Catchment Area Study data and reported that the lifetime prevalence of CFS was only 7 per 100 000. Gunn et al. (1933) also reported a similar low prevalence, i.e., 2.0–7.3 per 100 000, according to the 1988 CDC criteria from a physician-based survey in the USA. On the other hand, several recent community-based studies have reported higher prevalence rates: 0.1–0.2% in USA according to the 1988 CDC criteria, the British criteria (Jason et al. 1995) and the 1994 CDC criteria (Buchwald et al. 1995); 0.2% and 0.56% in UK according to their own criteria (Pawlikowska et al. 1994) and the British criteria (Lawrie and Pelosi 1995), respectively. These differences among studies are attributable to the criteria for CFS employed, study designs and study populations: Higher rates for British and 1994 CDC criteria (Bates et al. 1993; Wessely 1995); higher rates for a community-based survey than a physician-based survey, probably because some CFS patients did not visit physicians and physicians underdiagnosed the disorder (Jason et al. 1995). On the other hand, the prevalence of non-CFS chronic fatigue, i.e., chronic fatigue which lasted for a longer period but did not fulfil all criteria for CFS, in a community was reported as 2.3% (Buchwald et al. 1995) and 6% (Walker et al. 1993), much higher than those of CFS. It is suggested that CFS is distinct from non-CFS chronic fatigue and the prevalence of CFS is not high but at least 0.1% in a community population.

However, the prevalence of CFS in non-Western countries including Japan is still not clear. There might be ethnic difference in the prevalence of CFS (Gunn et al. 1993) and the formation of symptomatology of CFS might be affected by cultural background (Wessely 1995). The aim of the present study is to know the prevalence of CFS in a community population in Japan, based on a recent epidemiologic study of mental disorders in a community population in Japan (Fujihara and Kitamura 1993; Fujihara et al. 1994).

## SUBJECTS AND METHODS

### *Subjects*

All 18-year-old or above persons (230 males and 278 females) living in Town A in the Kofu-city (Yamanashi) were invited to participate in a baseline interview survey. A total of 207 subjects (41%) agreed to participate in the survey and were interviewed using a structured psychiatric diagnostic interview in November 1992. The respondents were also invited to participate in a follow-up interview survey approximately one year later. A total of 137 respondents (67% of the baseline respondents or 27% of the target population) were re-interviewed in August 1993. The respondents consisted of 60 males and 77 females. The average age  $\pm$  the standard deviation were  $59 \pm 15$  (range, 25–92) years old for males and  $55 \pm 16$  (range, 19–85) years old for females.

### *Methods*

The "Time-Ordered Stress and Health Interview" (TOSHI), a structured interview schedule, was employed to assess psychiatric disorders of each subject in the baseline survey (Kitamura 1992). Details about the interview schedule were described elsewhere (Aoki et al. 1994; Kawakami et al. 1996). This interview schedule was developed using wordings taken from a Japanese draft of the Composite International Diagnostic Interview (WHO 1990), the Schedule for Affective Disorders and Schizophrenia (Endicott and Spitzer 1978) and other structured interviews together with ad hoc items; and it was designed to make diagnoses of seven major mood and anxiety disorders, i.e., manic episode, major depressive episode, dysthymic disorder, generalized anxiety disorder, panic disorder, phobic disorders and obsessive-compulsive disorder, according to the Diagnostic and Statistical Manual 3rd Edition-Revised (DSM-III-R, American Psychiatric Association 1987).

The follow-up version of the TOSHI was employed in the follow-up survey to assess chronic fatigue and CFS, as well as major psychiatric disorders, during a nine-month period between November 1992 and August 1993. In addition to the standard questions for diagnosis of the seven DSM-III-R mood and anxiety disorders, we put a special set of questions in the interview schedule to assess chronic fatigue and CFS according to the 1988 CDC criteria for CFS (Holmes et al. 1988). Subjects were asked a screening question on whether they had experienced persistent or relapsing fatigue or easy fatigue for at least four days during the study period. If they had, then they were asked whether the fatigue reduced their daily activity 50% or more, which is required for the major criteria for CFS, and were asked about five of 11 symptom criteria for the CDC minor criteria: (1) prolonged fatigue over 24 hours after usual physical activity, (2) mild fever or chills, (3) painful lymph nodes in cervical or axillary distribution, (4) generalized muscle weakness, (5) muscle discomfort, (6) initial development of the fatigue and related symptoms within a few days. The remaining six symptoms in the symptom criteria were assessed elsewhere in the interview schedule: (7) sore throat, (8) headache, (9) pain in joints, (10) sleep disturbance (insomnia), (11) neuropsychologic complaints ([11a] irritability, [11b] loss of concentration or [11c] depression). Interviewers rated on each symptom only when it could not be explained by physical illness. Interviewers recorded the onset date and the recent date of the fatigue and the other symptoms. We did not evaluate three physical criteria (low-grade fever, non-exudative pharyngitis, palpable lymph nodes) which must be documented by physicians.

We trained 25 interviewers for the survey, which included psychiatrists, physicians, psychiatric social workers, clinical psychologists and postgraduate students in psychology and medicine. The training was offered for four days including didactic lectures and role playing. The interviews were made in the

regional mental health center or at the respondents' home. The procedures were fully explained to each subject before the survey and the written informed consent was obtained. Each interview took 1.5 to 2.5 hours for most cases.

Three different diagnostic criteria for CFS were applied: the 1988 CDC criteria (Holmes et al. 1988), the 1994 CDC criteria (Fukuda et al. 1994), and the British criteria (Sharpe et al. 1991). According to the 1988 CDC criteria, CFS was diagnosed when (a) a subject had fatigue for 6 months or longer which reduced his/her daily activity below 50% and could not be explained by other clinical conditions (major criteria) and (b) he/she had eight or more of the 11 symptom criteria (minor criteria). The 1994 CDC diagnosis was made when a subject fulfill the major criteria and had four of the following eight minor criteria: Loss of concentration, sore throat, painful cervical or axillary lymph nodes, muscle pain, pain in two or more joints, headache, sleep disturbance and prolonged fatigue over 24 hours after usual physical activity. A diagnosis of CFS according to the British criteria was made when a subject had chronic fatigue lasting for 6 months or more, substantial functional impairment (measured by 50% or more reduction of daily activity) and other symptoms (muscle pain, depression or sleep disturbance), but did not have diagnosed physical illness or a current diagnosis of the following psychiatric disorders: Manic depressive illness, substance abuse, eating disorder. Diagnoses of the seven mood and anxiety disorders during the past nine months, as well as lifetime diagnoses of nicotine and alcohol dependence, of each subject were made using the DSM-III-R criteria by the interviewer on the basis of presence/absence of the symptoms and were also checked by a psychiatrist. Lifetime history of the seven mood and anxiety disorders before November 1992 was made using the DSM-III-R criteria on the basis of the TOSHI data collected at the baseline survey. The point- and nine-month prevalence rates for each CFS diagnostic criteria were estimated. The 95% confidence intervals were calculated based on the binominal distribution (SAS Institute Inc. 1988).

## RESULTS

During the nine-month period, 3 of 137 respondents experienced fatigue for 2 weeks or longer which caused 50% or more reduction of daily activity (Table 1). Two of these cases (case A and B) had experienced chronic fatigue for 6 month or longer. None of these two cases fulfilled the 1988 CDC criteria for CFS, since they had only five or six of the 11 minor criteria symptoms. However, both of the two cases satisfied the 1994 CDC criteria and the British criteria for CFS. The point prevalence and the nine-month prevalence were both 1.5% with the 95% confidence intervals, 0.4-5.2%. However, neither of these cases had symptoms related to infection or inflammation, such as fever, sore throat and lymph node swelling.

TABLE 1. *Symptom profiles and diagnoses of CFS according to the 1988 CDC criteria, the 1994 CDC criteria and the British criteria in three cases among 137 respondents from a community-based interview survey in Japan\**

Criteria for CFS	Case A	Case B	Case C
	(Male, 29 years)	(Female, 37 years)	(Female, 20 years)
<b>Major criteria</b>			
Severe persistent fatigue			
Duration in months <sup>§</sup>	9+	200+	1.5+
50% or more reduced activity	yes	yes	yes
<b>Exclusion criteria</b>			
Physical illness known to cause chronic fatigue	no	no	no
Concurrent psychiatric disorder	no	no	Major depression
Previous psychiatric disorder	no	no	no
<b>Minor criteria</b>			
Mild fever	no	no	yes
Sore throat	no	no	yes
Painful lymph nodes	no	no	yes
General muscle weakness	yes	yes	yes
Muscle pain	yes	yes	yes
Prolonged fatigue for 24 hours or more	yes	yes	yes
Headache	yes	no	no
Pain in joints	yes	no	no
<b>Neuropsychological complaints</b>			
a. Irritability	no	no	yes
b. Loss of concentration	no	yes	yes
c. Depression	no	no	yes
Sleep disturbance	no	yes	no
Development within a few days	no	yes	no
<b>CFS diagnosis</b>			
1988 CDC criteria	no	no	no
1994 CDC criteria	yes	yes	no
British criteria	yes	yes	no

\* These cases had persistent fatigue for two weeks or more within a nine-month period (November 1992-August 1993).

§ “+” indicates that the fatigue symptom was still present on the survey day and might continue.

## DISCUSSION

We found a higher prevalence rate (1.5%) of CFS in a community population

in Japan according to the 1994 CDC criteria or the British criteria, compared with previous community-based studies in USA and UK, which reported 0.1–0.56% (Pawlikowska et al. 1994; Buchwald et al. 1995; Jason et al. 1995; Lawrie and Pelosi 1995). Our prevalence rate was even higher than the rates reported from primary care patients (i.e., 0.3–1.0%) (Bates et al. 1993). One limitation of our study is a lower response rate, which is only 27% of the initial target population. If people who had an experience of chronic fatigue were more willing to participate in the survey as a form of help-seeking, the prevalence rates might be overestimated. However, even when we suppose that there was no CFS case in the non-respondents, a conservative estimate of the prevalence is 0.4% (two of 508 residents) with the 95% confidence intervals of 0.1–1.4%. This is still higher than the rates from previous studies (Price et al. 1992; Buchwald et al. 1995; Jason et al. 1995), although it is very close to the rate from a questionnaire-based study in the UK (Lawrie and Pelosi 1995). It is suggested that CFS or an equivalent level of chronic fatigue is more prevalent in a community population in Japan.

Two cases diagnosed as CFS were relatively younger compared with the average age for the total respondents. This is consistent with previous findings (Bates et al. 1993; Jason et al. 1995). Although still inconsistent (Wessely 1995), a previous study has suggested that CFS is more prevalent in females than males (Pawlikowska et al. 1994). Neither of the two CFS cases had symptoms related to infection, such as fever, sore throat and painful lymph node, while both had symptoms related to fibromyalgia. Case definition of CFS by the 1988 and 1994 CDC criteria (Holmes et al. 1988; Fukuda et al. 1994) includes the presence of possible symptoms of infection as a minor criteria. A study of 51 clinical CFS patients in Japan (Nishikai 1992) reported that 63–71% of the patients had these infection-related symptoms. However, our findings suggest that CFS without symptoms of infection is much more prevalent in a general population. The discrepancy might be due to help-seeking behaviors associated with infectious symptoms. Since we had only two diagnosed cases, the symptom patterns and the frequencies should be examined in a future larger-scale study in community and clinical populations to develop a further classification of CFS.

The reason for the higher prevalence of CFS in our study is not clear. In a previous study, only one-tenth of those who fulfilled the major criteria (i.e., chronic fatigue lasting for 6 months or longer and reduced activity due to the fatigue) for CFS were diagnosed as CFS (Buchwald et al. 1995). On the other hand, all cases who met the major criteria were diagnosed as CFS in our study. The prevalence rate of CFS in our study is rather close to prevalence rates of non-CFS chronic fatigue (Walker et al. 1993; Buchwald et al. 1995). A possibility is that we might overestimate minor criteria symptoms in our assessment schedule. The 1988 and 1994 CDC criteria require that minor symptoms persisted or recurred for 6 months or longer (Holmes et al. 1988; Fukuda et al. 1994). We assessed the duration of each minor symptom, but we did not assess the frequency

of recurrence or the duration of the presence or absence of each episode for the minor symptoms. This might result in overestimation of the minor symptoms and, in turn, of the prevalence of CFS. However, this is not case for the British criteria which does not have a duration criteria for minor symptoms (Sharpe et al. 1991). Another possible explanation is a cross-cultural difference in symptom expression. It has been suggested that people in Asian countries tend to express their psychological distress as physical complaints (Kleinman and Kleinman 1985). Such tendency might results in a higher prevalence rate of CFS in Japan according to the diagnostic criteria developed in Western countries. Cross-cultural comparison of the symptomatology of CFS in both community populations and clinical patients between Western countries and Asian countries (including Japan) might be useful to clarify this possibility and develop a further diagnostic criteria for CFS.

Our study demonstrated a higher prevalence rate of CFS or chronic fatigue with an equivalent severity in a community population in Japan. The cases had severe fatigue symptom for a long duration and reduced their activities very much, suggesting a strong need for provision of health care service for these cases. However, a major limitation of our study was that the study was based on a small number of respondents; we could not provide a stable estimate of the prevalence of CFS. A larger-scale epidemiologic study is needed to estimate the prevalence of CFS, as well as non-CFS chronic fatigue, the risk factors and effects on people's life in Japan. Another problem was in an assessment method. We employed our own assessment schedule since no standardized interview schedule for CFS was available. The development of a reliable assessment instrument of CFS is needed for a future study. Accumulation of future evidence should be an indispensable step to determine the entity as a disorder and public health implication of CFS.

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