

# Chronic fatigue syndrome in Chinese middle-school students

Jieyao Shi, MD<sup>a,b</sup>, Jie Shen, MD<sup>c</sup>, Jian Xie, MD<sup>d</sup>, Jianming Zhi, MD, PhD<sup>e,\*</sup>, Yong Xu, MD<sup>a,\*</sup>

# Abstract

The objective of the present study was to determine the prevalence of chronic fatigue syndrome (CFS) and its associated factors in middle-school students in Suzhou, China. From September 2010 to January 2011, across-sectional study was conducted in juniorand senior middle-school students aged 10 to 18 years using a battery of confidential questionnaires. Our results indicate that 18,139 completed the questionnaires effectively, of whom 163 (0.9%) met the definition of CFS, with senior high-school students and male students predominating. The prevalence of CFS in the middle-school students increased steadily with age. The main symptoms of CFS in these students included being afraid of going to school, despondency, and irritability in addition to those specified in the Centers for Disease Control and Prevention (CDC). Our study shows that CFS is prevalent among Chinese teenagers, and requiring proper intervention and treatment.

**Abbreviations:** CDC = Centers for Disease Control and Prevention, CDC-94 = The US Centers for Disease Control and Prevention definition of CFS revised in 1994, CF = Chronic fatigue, CFQ = Chaldea fatigue scale, CFS = chronic fatigue syndrome, CIS = checklist individual strength, DSD = self-rating depression scale, GP = general practitioner, NF = no fatigue, SF-36 = MOS 36-item short-form health survey, SPSS = Statistical Package for Social Scientists.

Keywords: chronic fatigue syndrome, middle-school students, prevalence

## 1. Introduction

Chronic fatigue syndrome (CFS) is a complex multifactorial disorder and a public health problem and impose considerable burdens on society, families, and health service facilities.<sup>[1]</sup> Based on the data from the US Centers for Disease Control and Prevention (CDC), the impact of CFS on annual economy in the United States is estimated to be \$9.1 billion in lost productivity, not including medicinal costs or disability payments, and the average affected family forgoes approximately \$20,000 in annual income.<sup>[2]</sup> The clinical course of CFS is characterized by an intermittent pattern of relapse and remission, with a median recovery rate of 5% in adults.<sup>[3]</sup> The situation in children and adolescents seems more optimistic than that in adults. Some

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<sup>a</sup> Soochow University School of Public Health, <sup>b</sup> Suzhou Vocational University, <sup>c</sup> Suzhou Science & Technology Town Hospital, <sup>d</sup> Suzhou New District Health Inspection and Supervision Institution, Suzhou, <sup>e</sup> Department of Anatomy and Physiology School of Medicine, Shanghai Jiaotong University, Shanghai, China.

<sup>\*</sup> Correspondence: Jianming Zhi, Shanghai Jiao Tong University School of Medicine, Shanghai, Shanghai China (e-mail: zhijm@shsmu.edu.cn); Yong Xu, Soochow University School of Public Health, Suzhou, China (e-mail: xuyong\_1959@126.com).

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previous studies<sup>[4]</sup> reported that many children and adolescents could finally recover from CFS if they received appropriate treatment within 2 years from onset. However, recovery would be difficult if treatment is delayed for 5 years from onset, which underlines the importance of early detection of the disease.

CFS has been reported frequently in adults in the United States, UK, Australia, and Netherlands. However, reports about CFS in general Asian teenagers are extremely limited, especially in children and adolescents. The prevalence of CFS in children and adolescents elsewhere is about 0.0%1 to  $4.4\%^{[5-15]}$  (Table 1), indicating that CFS has become an increasingly severe public health event in recent years, and a common symptom in modern adolescent populations in China.

The aim of the present survey was to estimate the prevalence of CFS and its associated factors in middle-school students in Suzhou, China. The study would help gain insights into the mechanism underlying the illness and provide targets for the development or improvement of the existing therapeutic strategies for the sake of reducing the incidence of the persistent fatigue status in China.

# 2. Methods

#### 2.1. Survey in general

This cross-sectional survey enrolled 18,420 middle-school students aged 10 to 18 years (mean  $14.9 \pm 1.68$ ) who were selected randomly between September 2010 and January 2011 from 25 junior- and senior-middle schools in Suzhou, China at a ratio of 1:1 with respect to the gender and grade. Information regarding fatigue and associated symptoms, demographic characteristics, and medical histories including depression and physical function was obtained by a battery of confidential questionnaires completed by the students personally with the help from trained investigators. The data were coded by using Lauritsen JM & Bruus M. EpiData (version 3). Of the 18420

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Review of epidemiological studies on CFS in children and adolescents.

| Subject         | Criteria   | Area         | Participants         | Age   | CFS, %            | CF, % | Ref |
|-----------------|------------|--------------|----------------------|-------|-------------------|-------|-----|
| School          | CDC-94,CFQ | China        | 18,139               | 10–18 | 1.80              | 12.0  | *   |
| Community       | CDC-94     | USA          | 2249                 | 2–17  | 0.04              | 0.22  | 10  |
| Population      | CDC-94     | USA          | 8586                 | 12–17 | 0.01              | 1.20  | 5   |
| Population-twin | CDC-94     | Austrian, UK | 99                   | 8–17  | 1.29              | -     | 7   |
| GP              | CDC-94     | Netherland   | 304                  | 10–18 | 0.11              |       | 9   |
| Primarycare     | CDC-94,CFQ | USA          | 901                  | 11–18 | 4.40              | -     | 6   |
| Community       | CDC-94     | UK           | 4240                 | 11–15 | 0.19              | 0.60  | 11  |
| GP              | Oxford     | UK           | 1024                 | 5–19  | 0.06              | -     | 12  |
| School          | CIS,CFQ    | Japan        | 1225                 | 11–16 | -                 | 1.20  | 13  |
| Population      | CDC-94     | USA          | 16,970 <sup>‡</sup>  | <18   | 0.06              | -     | 8   |
| Population      | CDC-94     | USA          | 12,000 <sup>§</sup>  | 5–17  | 2.05 <sup>†</sup> | -     | 14  |
| Community       | Austrian   | Austrian     | 114,000 <sup>‡</sup> | 10–19 | 0.48              | _     | 15  |

CFS = chronic fatigue syndrome, CDC-94 = US Centers for Disease Control and Prevention definition of CFS revised in 1994, CFQ = Chaldea fatigue scale; CIS = checklist individual strength, GP = general practitioner, -= no data, Ref = reference.

\* The present study

<sup>+</sup> cfs-like illness

<sup>‡</sup> The number of included population both adolescents and adults.

§ The number of included households

initially included students, 281 (1.5%) students were excluded because they failed to complete the questionnaires or provide reliable information. Finally, 18,139 students were included for analysis. The Statistical Package for Social Scientists (SPSS 19.0) was used for all analyses unless otherwise noted. Using frequency descriptive statistics, Chi-squared test and t test, differences in demographics were compared between the groups. The results of hypothesis test are expressed as exact P values, and P values below 0.05 indicate significant differences in variable analysis.

#### 2.2. Assessment instruments and case identification

The severity of fatigue-related symptoms was assessed according to the US CDC-94 definition of CFS,<sup>[1]</sup> and the Chaldea fatigue scale (CFQ).<sup>[16]</sup> For further characterization, all the students were also asked to complete the MOS 36-item short form health survey (SF-36) to define the physical function,<sup>[17]</sup> and self-rating depression scale (DSD) to identify the depressive symptoms.<sup>[18]</sup> Twelve associative symptoms of children and adolescents screened from previous studies were included to explore the special nature of children and adolescents with CFS.<sup>[19–22]</sup>

Although the CDC-94 is not a "good standard" to assess CFS for self-reported criteria, it is the only accepted guideline for case definition at present. In addition, most symptoms of CFS occurring in children and adolescents are similar to those seen in adults.<sup>[23]</sup> According to the CDC-94, CFS occurs when a person experiences fatigue for 6 months or is accompanied with at least 4 of the 8 CFS symptoms. It is important that each symptom should be rated frequently or constantly to meet the criteria, but this "persistence index" has not been well defined in previous criteria. In the present study, we defined these symptoms as 1, not present; 2, occasionally present; 3, sometimes present; 4, frequently present; and 5, always present. As the CDC-94 does not specify how to assess the severity of fatigue, we included the CFQ in the survey to investigate its usefulness for epidemiological research.<sup>[6,13]</sup>

The CFQ is a self-report questionnaire inquiring about various physical and mental fatigue symptoms specifically related to fatigue, and has been validated in large community samples.<sup>[24]</sup> It consists of 11 items rated on four options: 0, better than usual; 1,

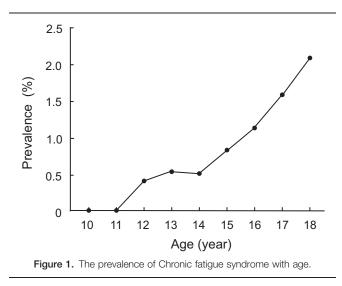
no more than usual; 2, worse than usual; and 3, much worse than usual, using a bimodal response system (0, 0, 1, 1) with a score range from 0 to 11. Despite its brevity, it has been found to be a reliable and valid Chinese version with sufficient internal consistency (Cronbach's alpha=0.86),<sup>[25]</sup> and the factor structure of the original version was replicated.<sup>[26]</sup> An overall CFQ score  $\geq 4$  and duration of symptoms  $\geq 3$  months represent persistent fatigue, whereby it should be able to differentiate a sample with CFS from a healthy sample. The limitations of the CFQ include its inability to distinguish between CFS and primary depression.<sup>[26]</sup> The detailed status between depression and CFS will be further discussed in other articles of this study, knowing that the relationship between them is complex, and that depression co-exists commonly with CFS.

CFS was defined if the subjects met the criteria of both CDC-94 and CFQ, and at the same time the school health workers excluded the fatigue symptoms that may be associated with other medical conditions after reviewing their yearly routine physical examination records. Those who reported chronic fatigue but failed to meet the CDC-94 and CFQ criteria were diagnosed as having chronic fatigue (CF), and those who met none of the criteria were diagnosed as having no fatigue (NF).

The 12 associative symptoms of children and adolescents, including diarrhea, feverishness, rash, abdomen pain, constipation, sensitivity to light, being afraid of going to school, newonset allergy, despondency, eating more than before, unwillingness to eat, and irritability were screened from previous studies in children and adolescents.<sup>[11–14]</sup> The validity of all symptoms was assessed with sensitivity, specificity, and Youden's index. Validity means the degree to which the measured result corresponds to the actual value. It is evaluated by sensitivity, specificity, and Youden's index.

#### 2.3. Ethics consideration

The participants or/and their guardians were informed of the study aims and methods using a leaflet. Patients were free to participate or refuse without consequences. All participants or/ and their guardians provided written consent before entry into the study. The research protocol was approved by the ethics committee of Soochow University.



# 3. Results

#### 3.1. Prevalence estimates

All the 18,139 subjects completed the detailed questionnaire efficiently. The prevalence of CFS and CF in this study was 0.9% and 12.0%, respectively. The prevalence of CFS increased steadily with age (Fig. 1). Table 2 shows the prevalence of CFS for demographic subgroups. The prevalence of CFS in the senior middle-school students was significantly higher than that in the junior middle-school students (Chi-square test, P < .001). There was significant gender difference in CFS prevalence with a male/ female ratio of 1/0.87.

#### 3.2. Symptoms

Other than fatigue, muscle pain, joint pain, difficulty in concentration, headache, and sore throat as specified in the CDC-94, despondency, irritability and being afraid of going to school were the most important symptoms of CFS in the middle-school students investigated in this study (Table 3). The validity of un-refreshing sleep and lymph node tenderness as specified in the CDC-94 was relatively low in the present study, and was even lower than that of the 12 associative symptoms in children and adolescents.

| Comparison on the demographic characteristics between group |                       |                      |                            |  |  |  |
|---|-----------------------|----------------------|----------------------------|--|--|--|
| Characteristic  | NF group<br>(n=15627) | CF group<br>(n=2183) | CFS group<br>(n=163)       |  |  |  |
| Grade, %  |                       |                      |                            |  |  |  |
| Junior high school  | 50.7                  | 33.6*                | 24.7 <sup>*,†</sup>        |  |  |  |
| Senior high school  | 49.3                  | 66.4*                | 75.3 <sup>*,†</sup>        |  |  |  |
| Area, %   |                       |                      |                            |  |  |  |
| Metropolitan  | 48.7                  | 48.6                 | 53.8                       |  |  |  |
| Town  | 51.3                  | 51.4                 | 46.2                       |  |  |  |
| Gender, %   |                       |                      |                            |  |  |  |
| Male  | 49.3                  | 45.9 <sup>*</sup>    | 53.5 <sup>*,†</sup>        |  |  |  |
| Female  | 50.7                  | 54.1 <sup>*</sup>    | 46.5 <sup>*,†</sup>        |  |  |  |
| Age (mean $\pm$ SD)   | 14.83±1.66            | $15.37 \pm 1.57^{*}$ | 15.71 ± 1.53 <sup>*,</sup> |  |  |  |

Statistical analysis was performed using Chi-square and t test.

CF=chronic fatigue, CFS=chronic fatigue syndrome, NF=no fatigue.

P<.01 vs NF group.

 $^{+}P$  < .01 vs CF group.

# Table 3

Validity of symptoms for children and adolescents with chronic fatigue syndrome.

| Symptoms                | Sensitivity,<br>% | Specificity,<br>% | Youden's<br>index, % |  |
|-------------------------|-------------------|-------------------|----------------------|--|
| CDC-94 symptoms         |                   |                   |                      |  |
| Postexertion malaise    | 99.4              | 46.1              | 45.5                 |  |
| Unrefreshing sleep      | 20.7              | 86.0              | 6.7                  |  |
| Concentrating           | 71.4              | 93.8              | 65.2                 |  |
| Muscle pain             | 77.5              | 93.9              | 71.4                 |  |
| Joint pain              | 73.0              | 96.1              | 69.1                 |  |
| Sore throat             | 63.2              | 94.4              | 57.6                 |  |
| Headache                | 65.0              | 95.4              | 60.4                 |  |
| Tender lymph nodes      | 28.9              | 98.4              | 27.3                 |  |
| 12 symptoms             |                   |                   |                      |  |
| Diarrhea                | 21.9              | 97.2              | 19.1                 |  |
| Feverishness            | 23.4              | 98.5              | 21.9                 |  |
| Rash                    | 16.4              | 98.3              | 14.7                 |  |
| Abdomen pain            | 32.2              | 96.9              | 29.1                 |  |
| Constipation            | 20.7              | 97.2              | 17.9                 |  |
| Sensitivity to light    | 34.7              | 95.6              | 30.3                 |  |
| Afraid of school        | 53.8              | 91.9              | 45.7                 |  |
| New atopic              | 29.2              | 97.3              | 26.5                 |  |
| Despondency             | 73.3              | 88.3              | 61.6                 |  |
| More eating than before | 32.5              | 87.8              | 20.3                 |  |
| Unwilling to eat        | 46.5              | 92.6              | 39.1                 |  |
| Irritability            | 57.8              | 89.6              | 47.4                 |  |

CDC-94 = The US Centers for Disease Control and Prevention definition of CFS revised in 1994.

#### 4. Discussion

#### 4.1. Prevalence of CFS

Most studies on CFS have focused on adults in clinical settings, and few studies have focused on children and adolescents. As shown in Table 1, the reported prevalence of CFS in children and adolescents varies greatly from 0.01% to  $4.4\%^{[5-15]}$  versus 0.9%in the present study, which is significantly lower than the result reported by Mear et al,<sup>[6]</sup> similar to that reported by Farmer et al,<sup>[7]</sup> and significantly higher than that reported by Jones et al<sup>[5]</sup> and Steele et al<sup>[8]</sup> in the United States. All together, the prevalence of self-reported fatigue varies widely, because people tend to define it accordingly.<sup>[27]</sup> Studies based on questionnaire assessment seem to yield higher prevalence than those based on interviews.<sup>[8]</sup> A direct comparison of this study with the results of previous studies is nonetheless difficult because of lacking a consistent standard definition and differences in study populations, sampling strategies, and statistical methods for estimating the prevalence. Compared with most studies in other countries, CFS seems to be a more serious problem in the children and adolescents in Suzhou, China. Whether this tendency can represent the general situation in China requires more coordinative surveys covering larger areas and more populations. At current stage, little attention has been paid to CFS in China, especially in children and adolescents. One reason is that most Chinese people and families know little about CFS. In addition, it is often misdiagnosed as a psychological problem, or even misdiagnosed or maldiagnosed as general fatigue. Another reason is that there are no specific criteria for the diagnosis of CFS. As the onset of CFS is usually insidious and related symptoms vary greatly, it is often difficult to detect it early. Past experience has shown that epidemiological research can help the prevention and control of the disease.

#### 4.2. Characteristics of symptoms

Although fatigue is the most important symptom in both adolescents and adults, accounting for 99.4% in this study, children and adolescents may experience different symptoms as compared with adults with CFS. Symptoms such as rash and abdominal pain may be frequently present in children and young adolescents, but may not be as common in adults. Our study found that being afraid of going to school, despondency and irritability are 3 major specific symptoms of CFS in children and adolescents. Pelcovitz et al also found that Being afraid of going to school is a major symptom.<sup>[19,28]</sup> Despondency is the same as the finding of Chalder et al.<sup>[29]</sup> and Emslie et al.<sup>[30]</sup> Irritability is similar to the report of De Meirleir et al.<sup>[31]</sup> In addition, unrefreshing sleep and lymph node tenderness, 2 symptoms frequently present in adults with CFS, are uncommon in children and young adolescents with CFS. Therefore, it should be prudent to directly use the CDC-94 criteria for adults to assess CFS in children and young adolescents, although it is used widely in CFS study.

# 5. Conclusions

The data obtained from the present study provide important information for further study of CFS in children and young adolescents in China as a whole. In addition, the specific symptoms in CFS children and young adolescents provide valuable references for defining the diagnostic criteria of CFS in children and adolescents in China, and other countries and regions as well.

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