

1 **Prevalence of depressive symptoms and related risk factors in Japanese patients**
2 **with pulmonary nontuberculous mycobacteriosis**

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Abstract

The objective of this study was to administer commonly used tools, the Center for Epidemiological Studies Depression Scale (CES-D) and the Hospital Anxiety and Depression Scale - Depression subscale (HADS-D), to screen for depressive symptoms in patients with nontuberculous mycobacterial pulmonary disease (NTM-PD). In addition, we sought to identify whether differences existed in the prevalence of depressive symptoms as assessed by CES-D and HADS-D, and by various predictors of depression.

The presence of depressive symptoms in 95 patients with NTM-PD was assessed using the CES-D and HADS-D. Data regarding age, body mass index, pulmonary function, dyspnea, cough, and exercise capacity were obtained to examine their independent contribution as predictors of depressive symptoms.

The prevalence of depressive symptoms was 37.9% based on CES-D and 26.3% based on HADS-D. The prevalence of depressive symptoms based on CES-D and HADS-D revealed significant differences between the two instruments. Analysis suggested that the presence of cough is a significant predictor of depressive symptoms as assessed by both CES-D and HADS-D.

Countermeasures are necessary because some patients with NTM-PD disease have depressive symptoms. It is possible that assessment of the prevalence of depressive symptoms differs in accordance with the screening tool used.

Keywords: Center for Epidemiological Studies Depression Scale, depressive symptom, Hospital Anxiety and Depression Scale, nontuberculous mycobacterial pulmonary disease, prevalence.

1 **Introduction**

2 In recent years, cases of nontuberculous mycobacterial pulmonary disease (NTM-PD)
3 have increased worldwide (Diel et al., 2017; Haworth et al., 2017; Prevots & Marras,
4 2015). Compared to global prevalence rates, the prevalence of NTM-PD in Japan is higher
5 (Namkoong et al., 2016). NTM-PD is a chronic disease that requires long-term treatment
6 (Henkle et al., 2016), with patients said to experience negative emotions during this time
7 (Henkle et al., 2016). Mental health issues of patients, such as anxiety and depressive
8 symptoms, raise concerns for treatment adherence as these patients often have reduced
9 medication compliance (Quittner et al., 2016; Quittner et al., 2014). For these reasons,
10 studies related to the evaluation of depressive symptoms and reduction of those symptoms
11 are viewed as one of the priority research areas for NTM-PD in the future (Henkle et al.,
12 2016).

13 As with chronic obstructive pulmonary disease (COPD) (Matte et al., 2016) and
14 pulmonary tuberculosis (Dasa et al., 2019; Duko, Gebeyehu, & Ayano, 2015; Gong et al.,
15 2018; Koyanagi et al., 2017; Sulehri, Dogar, Sohail, Mehdi, & Azam, 2010) patients,
16 individuals with NTM-PD experience depressive symptoms as well. Further, the
17 prevalence of depressive symptoms may vary depending on the screening tool used.
18 However, there are few reports of studies with NTM-PD patients. In the future, screening
19 for depressive symptoms and countermeasures to treat these symptoms may be necessary

1 to maintain good medication compliance and quality of life for patients with NTM-PD.

2 The objective of this investigation was to examine the prevalence of depressive
3 symptoms in individuals with NTM-PD and to determine if the prevalence of depressive
4 symptoms differs according to assessment with two well-known screening tools (Center
5 for Epidemiological Studies Depression Scale (CES-D) and the Hospital Anxiety and
6 Depression Scale - Depression subscale (HADS-D)). Second, the study aimed to
7 determine factors related to the prevalence of depressive symptoms.

8

9 **Methods**

10 Participants were 95 patients with a medical diagnosis of NTM-PD at Fukujuji Hospital
11 in Japan between December 2016 and August 2019. The study was approved by the Ethics
12 Committee of Fukujuji Hospital (approval number: 19011).

13 In this study, two screening tools for depressive symptoms, Japanese versions of the
14 CES-D and the HADS, were used (Hatta et al., 1998 (in Japanese); Zigmond & Snaith,
15 1983). CES-D and HADS score suggests the presence of clinical depression symptoms;
16 however, this score does not allow for a diagnosis of depression to be made. The following
17 data were also collected: gender, age, body composition (body mass index [BMI]),
18 pulmonary function, dyspnea (modified Medical Research Council dyspnea scale

1 [mMRC]), cough symptoms (Leicester Cough Questionnaire [LCQ]), and exercise
2 capacity (Incremental Shuttle Walking Test [ISWT]).

3 Dyspnea was evaluated using the mMRC dyspnea scale, which grades the severity of
4 dyspnea during daily living from grade 0 to grade 4 (Mahler & Wells, 1988). Cough
5 symptoms were evaluated using the LCQ, which is a brief, easy-to-administer, and well-
6 validated cough-specific health-related quality-of-life questionnaire (Birring et al., 2003).
7 In this study, participants were classified into four groups based on the LCQ quartiles,
8 ranging from low scores with poor health, due to cough symptoms, to high scores with
9 good health (LCQ1, LCQ2, LCQ3, LCQ4).

10 The prevalence of depressive symptoms in NTM-PD patients was determined by
11 calculating the percentage of participants exhibiting a score of 16 points or higher on the
12 CES-D and 8 points or higher on the HADS-D among the total number of participants.
13 McNemar's test was used to determine whether there was a significant difference in the
14 prevalence of depressive symptoms based on each scale. To evaluate the consistency in
15 the prevalence of depressive symptoms assessed utilizing the two scales, correlational
16 analyses involving the total scores for each scale were performed using Spearman's
17 correlation coefficients. In addition, to clarify the characteristics of each scale, the Mann-
18 Whitney *U* test was used to compare between patients grouped according to the presence

1 or absence of depressive symptoms. The correlations between dyspnea and cough severity
2 and the existence of depressive symptoms were also examined using Fisher's exact test.
3 Logistic regression analysis was conducted to determine predictors of depressive
4 symptoms as determined by HADS-D and CES-D.

5

6 **Results**

7 The clinical characteristics of all participants are shown in Table 1. The percentage of
8 patients who were judged as having depressive symptoms based on the scores of each
9 scale was 37.9% ($n = 36$) for CES-D and 26.3% ($n = 25$) for HADS-D ($P = 0.035$).

10 The relationships between participant characteristics and evidence of depressive
11 symptoms are presented in Table 2. For both CES-D and HADS-D, patients with
12 depressive symptoms had significantly higher mMRC scores and lower LCQ scores
13 compared to those without depression. Figure 1 displays the prevalence of depressive
14 symptoms with respect to dyspnea severity for CES-D and HADS-D. Figure 2 displays
15 the prevalence of depressive symptoms with respect to cough severity for CES-D and
16 HADS-D. With both scales, there was a positive relationship between greater depressive
17 symptoms and increasing severity of dyspnea and cough.

18 The results of the logistic regression analysis are presented in Table 3. For both CES-

1 D and HADS-D, LCQ exerted an effect such that depressive symptoms were more likely
2 to occur in patients with a low LCQ, indicating more severe cough symptoms.

3

4 **Discussion**

5 Although estimates of prevalence vary across countries, in many locations, the lifetime
6 prevalence of depression ranges from 8% to 12% (Andrade et al., 2003). Similar to the
7 findings in patients with COPD (Matte et al., 2016) and tuberculosis (Gong et al.,
8 2018);(Duko et al., 2015), the prevalence of depressive symptoms in patients with NTM-
9 PD in this investigation was 37.9% for CES-D and 26.3% for HADS-D, which is higher
10 than that in the general population.

11 In this study, cough symptoms were associated with depressive symptoms in patients
12 with NTM-PD, regardless of age, BMI, dyspnea, and exercise capacity. Given that cough
13 symptoms are the most common symptoms experienced in patients with NTM-PD
14 (Dailloux et al., 2006; Koh et al., 2012), it is possible that coughing may result in
15 depressive symptoms.

16 In patients with NTM-PD, a screening test for depressive symptoms and treatment for
17 depressive symptoms are necessary to maintain good patient health and improve
18 treatment outcomes. Dicipinigaitis et al. reported a significant correlation between

1 improvement of cough symptoms and improvement of depressive symptoms
2 (Dicpinigaitis, Tso, & Banauch, 2006). Chest physical therapy has been shown to reduce
3 cough and sputum symptoms of individuals with NTM-PD (Basavaraj et al., 2017).
4 Psychological care is effective in improving depressive symptoms (Dicpinigaitis et al.,
5 2006) and is also important in the treatment of physical diseases (Prince M et al., 2007).
6 If screening tests are performed on patients with NTM-PD and patients with depressive symptoms are
7 identified, the need for physical therapy for coughing as well as consultation with a psychiatric
8 specialty commission should be considered. To date, few studies have examined depressive
9 symptoms in patients with NTM-PD. The present investigation is significant as one of the
10 few epidemiological studies to clarify the prevalence of depressive symptoms in Japanese
11 patients with NTM-PD.

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