Screening of depression and anxiety in cystic fibrosis patients/caregivers and evaluation of risk factors

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Abstract

Background: Depression and anxiety symptoms in patients with cystic fibrosis (CF) and their caregivers are 2-3 times higher than in the normal population. This study aims to evaluate the frequency and severity of depression and anxiety symptoms and to determine possible risk factors in CF patients and their mother and/or fathers at Marmara University CF center. Methods: The study included 132 CF patients who were followed up at our CF center. Patient Health Questionnaire (PHQ-9) and the Generalized Anxiety Disorder Questionnaire (GAD-7) were used to screen depression and anxiety. The questionnaires were completed by 50 CF patients (aged 12 - 17 years) and 132 parents of patients (aged 0-17 years). Results: While moderate to severe depression were seen in 25.5% of patients, 33.7% of mothers and 14.6% of fathers; moderate to severe anxiety were present in 17.6%, 21.8% and 8.5%, respectively. None of the demographic characteristics was identified as a predictor of depression or anxiety. GAD-7 scores have shown a higher incidence of anxiety in mothers of patients with chronic methicillin-resistant Staphylococcus Aureus ($p = 0.034$). Additionally, hospitalization in the last 12 months was statistically significantly higher in PHQ-9 scores of fathers ($p = 0.043$). Analysis of patients' adherence to medical treatment and airway clearance showed higher depression and anxiety in mothers of the non-adherent group ($p = 0.002$). Conclusion: Depression and anxiety were common in CF patients and their parents. These results illustrate the importance of depression/anxiety screening and psychosocial support for the CF patient and their parents.

Abbreviations:

CF: Cystic Fibrosis

PHQ-9: Patient Health Questionnaire

GAD-7: Generalized Anxiety Disorder Questionnaire

TIDES: The International Depression Epidemiological Study

ICMH: The International Committee on Mental Health in Cystic Fibrosis

ECFC: European Cystic Fibrosis Society

Introduction

Cystic fibrosis (CF) is the most common autosomal recessive disease that leads to early mortality in Caucasians worldwide [1]. The disease is highly burdensome with progressive multisystem involvement, mostly

problematic due to persistent lung infections, frequent hospitalizations and time consuming treatment regimens taking 2 to 4 hours per day in average [1; 2]. Numerous studies indicate that children and adults with chronic illnesses, as well as parent caregivers, are at increased risk for psychological difficulties .

The largest psychological screening study conducted on CF, The International Depression Epidemiological Study (TIDES), shows that rates of depression among patients are two times and parents of children with CF are 2-3 times higher than rates of depression in broad community samples [4]. Psychological distress in individuals with CF has been associated with: worse health outcomes (e.g., decreased lung function, lower BMI), worse adherence, worse quality of life, increased exacerbations, hospitalizations, and healthcare costs[5-8]. With these facts, The International Committee on Mental Health in Cystic Fibrosis (ICMH) developed consensus statements for screening and treating depression and anxiety in individuals with CF and their caregivers. The CF Foundation and European Cystic Fibrosis Society (ECFC) recommend 9-item Patient Health Questionnaire Depression Scale (PHQ-9) and 7-Item Generalized Anxiety Disorder Scale (GAD-7) for screening [9].

Despite evidence in the TIDES study that a new diagnosis of CF-related diabetes, and events such as hemoptysis and pneumothorax, may precede elevations in symptoms of depression and anxiety, little is also known about the 'triggers' of psychological symptoms, or how mood affects health outcomes in this complex disease. Therefore, ICMH suggested further studies to identify psychosocial and clinical risk factors of depression and anxiety in CF patients and their caregivers[9].

In the present study, we aimed to assess the prevalence of depression and anxiety in CF patients and parent caregivers along with identifying possible risk factors.

Methods

This is a cross-sectional single center study conducted at Marmara University Medical Faculty, Division of Pediatric Pulmonology Selim Çöremen CF Center between May 2019 and July 2019.

Participants were asked to complete the PHQ-9 and GAD-7 questionnaires to evaluate the level of their depression and anxiety at the outpatient clinic during routine follow-up visit. Patients with a definitive diagnosis of CF were eligible. Consecutive sampling method was used and all patients who came to the outpatient clinic during the study period were involved into the study.

The objectives of this study are to measure depression and anxiety levels of patients and their caregivers and to determine the risk factors affecting these levels. Patients' signs and symptoms were noted before the questionnaires were done. Necessary information for evaluation of the clinical status of the patient and adherence to medical treatment/airway clearance were collected from medical records. Adherence was assessed by patient/parent self-reports. Patients' age, age at the time of diagnosis, anthropometric measurements, mutations, forced expiratory volume in one second (FEV1) %, treatment and pulmonary physiotherapy regimens, past medical history (allergic bronchopulmonary aspergillosis, pneumothorax, hemoptysis, number of hospital admissions and exacerbations, sputum colonization history) and co-morbidities were noted for analysis. CF disease severity was classified as mild if the FEV1 was more than 70%, as moderate if the FEV1 was between 40% and 69.9%, and as severe if the FEV1 was 39.9% or below of the predicted value.

For the assessment of anxiety and depression, participants were asked to complete the validated Turkish versions of 9-item Patient Health Questionnaire Depression Scale (PHQ-9) and 7-Item Generalized Anxiety Disorder Scale (GAD-7)[10]. The PHQ-9 is composed of nine depressive symptom items listed in the Diagnostic and Statistical Manual of Mental Disorders-4th edition (DSMIV) for depression. Patients were asked to rate the extent of their symptoms that had bothered them during the previous 2 weeks using a 4-point Likert rating scale. The PHQ-9 severity score ranges from 0 to 27. Patients achieving a score equal or above 15 are regarded as suffering from at least minor depression [11].The GAD-7 is a tool to assess general anxiety disorder and it is comprised of seven items representing the DSM-IV symptom criteria for GAD (e.g., "Feeling nervous, anxious or on edge").

Patients were asked to indicate how often, during the last 2 weeks, they were bothered by each symptom,

using a 4-point Likert-type rating scale. Total test scores range from zero to 21 with a score of eight deemed sufficient to identify symptoms of general anxiety disorder, panic disorder, post-traumatic stress disorder or social anxiety disorder[12]. The internal consistency reliability of the Turkish version of the GAD-7 (Cronbach's $\alpha = 0.85$) and the test–retest reliability (intraclass correlation = 0.83) were reported to be good[12; 13].

The aim of the study was explained and informed consent was obtained from the participants beforehand. The Marmara University Medical Faculty Research Ethics Committee had approved the study, protocol number 09.2020.510.

Statistical analysis

Data were analyzed using the Statistical Program for Social Sciences (SPSS for IBM, 21.0). Descriptive statistics are presented in numbers, mean and standard deviations. The normal distribution of continuous variables was evaluated using the Shapiro-Wilk test. The Mann–Whitney U test was used for group comparison and the Spearman's rho correlation coefficient to assess relationships. $p < 0.05$ was used for statistical significance.

Results

Demographics and medical data

50 adolescents with CF (aged 12–17 years) and parents of 132 CF patients aged 0 - 17 (94 mother and 48 father) were asked and all agreed to participate in the study. Patients' characteristics are presented in Table 1.

Prevalence of anxious and depressive symptoms in adolescent CF patients (aged 12-17) (N=50)

The mean scores of 50 patients aged 12-17 years old were 7.71 ± 4.85 for PHQ-9 and 5.55 ± 3.83 for GAD-7. PHQ-9 scores showed nearly $\frac{1}{4}$ of patients (25.5%) had moderate to severe depression. Anxiety symptoms were less frequent than the depressive symptoms with no patients reporting severe anxiety and 17.6% reporting moderate anxiety (Table 2).

Additionally, there was a significant correlation between depression (PHQ-9) and anxiety (GAD-7) scores in adolescent patients (r = 0.655 p = 0.000)

Prevalence of anxious and depressive symptoms in parents of CF patients

The mean scores of both depression and anxiety were higher in mothers compared to fathers ($p < 0.05$). The mean PHQ-9 scores were 7.99 ± 4.65 in mothers and 5.73 ± 3.66 in fathers, while GAD-7 scores were 6.60 ± 4.42 and 4.09 ± 3.63, respectively. Results of the questionnaires show 33.7% of mothers and 14.6% of fathers had moderate to severe depression. Moreover, 21.8% of mothers and 8.5% of fathers had moderate to severe anxiety (Table 2). There were statistically significant correlations between PHQ-9 and GAD-7 scores in both mothers (r = 0.734 p = 0.000) and fathers (r = 0.706 p = 0.000).

Determinants of depression and anxiety in adolescent CF patients

There was no difference in depression and anxiety scores between male and female patients. Having comorbidities (CF related diabetes mellitus (CFRD), hepatobiliary disease, BiPAP or oxygen use, pancreatic

insufficiency and/or allergic bronchopulmonary aspergillosis (ABPA) did not show any statistically significant difference in depression or anxiety scores ($p > 0.05$).

Patients' age, age at diagnosis, BMI z-score, disease severity, number of hospitalization and exacerbations in the last year and FEV1% predicted was not significantly correlated with anxiety or depression ($p > 0.05$) (Table 3).

Chronic pulmonary infection with Pseudomonas aeruginosa (Pa) or Methicillin-resistant Staphylococcus Aureus (MRSA) were not associated with depression or anxiety in this patient group ($p > 0.05$). Table 3 presents the Spearman's rho correlation coefficients.

Determinants of depression and anxiety in parents of CF patients

Gender, age, BMI z-score, age at diagnosis, disease severity, FEV1% predicted and number of exacerbations in the last year did not show any difference in depression and anxiety of parents (Table 3). Additionally, having comorbid disorders such as CFRD, hepatobiliary disorder, ABPA, pancreatic insufficiency and BiPAP or oxygen use were not significantly different ($p > 0.05$). However, the results show a statistically higher anxiety score (GAD-7) in mothers of patients with chronic MRSA infection ($p = 0.034$). Moderate to severe anxiety rates were 46.2% and 17.8% in mothers of patients with and without chronic MRSA infection, respectively. Further analysis of the patients with chronic MRSA infection, number of exacerbations in the last year ($p = 0.046$) and number of hospitalizations in the last year ($p = 0.012$) were statistically higher compared to patients without chronic MRSA infection. On the other hand, while FEV1 was lower in the group with chronic MRSA infection, it was not statistically significant ($p = 0.385$). Moreover, fathers of patients who had hospitalized at least once in the last year had higher levels of depression in results of PHQ-9 ($U = 190.5$, $p = 0.043$).

Patients' adherence with medical treatment and airway clearance adherence

There was no significant association found between patient's adherence to medical treatment/airway clearance and PHQ-9 or GAD-7 scores of patients and fathers. There was a significant difference between both PHQ-9 ($p = 0.002$) and GAD-7 ($p = 0.002$) scores of mothers and patient adherence. In both, test scores were significantly higher in non-adherent group, meaning worse depression and anxiety symptoms. Figure 1 and Figure 2 shows the distributions and mean ranks of each group.

Discussion

Recent studies show significant increase in symptoms of depression and anxiety among CF patients and parent caregivers worldwide. Latest guidelines on CF care recommend screening of depression and anxiety symptoms in routine care of the patients [4; 9; 14]. This study aimed to determine the prevalence of depression/anxiety and possible risk factors in a single CF Center. To the best of our knowledge, this is the first study evaluating the prevalence of depression and anxiety in CF by using PHQ-9 and GAD-7 in Turkey. The present findings show a high prevalence of depression and anxiety in both adolescent CF patients and parents of CF patients.

Our data showed that quarter of the adolescent CF patients (25.5%) had moderate to severe depression. The largest international screening study (TIDES) reported depression among adolescents between 5-19%. A cross-sectional study conducted in Turkey compared depression and anxiety in 35 CF patients and 40 healthy control group by the Child Depression Inventory (CDI) and the State-Trait Anxiety Inventories for Children (STAI-C) [15]. In this study, Senses-Dinc et al. have found that the depression and anxiety symptom levels were significantly greater and the quality of life scores were significantly lower in CF than the healthy controls [15]. Another study on Turkish CF patients demonstrated that the individuals with CF who were diagnosed with major depression (measured by CDI) outnumbered those in control group (21.9% vs 6.1%), although the difference was not statistically significant [16].

According to TIDES study, 22% of adolescent CF patients had elevated symptoms of anxiety. Our data showed moderate to severe anxiety in more than one-sixth (17,6%) of patients. Gundogdu et al. reported 46.9% vs 15.2% general anxiety disorder in CF and control groups respectively, however when they compared the subgroups of anxiety disorders, the differences between the groups reached statistical significance only for specific phobia (related to medical procedures, such as the placement of feeding tubes and the insertion of central catheters)[16].

None of the predictors such as BMI z-score, age at diagnosis, disease severity, FEV1% predicted and number of exacerbations in the last year studied in this research was associated with different rates of depression or anxiety in adolescent patients. Quittner et al. published the following characteristics associated with increased symptoms of depression: being female, an episode of hemoptysis/pneumothorax in past 6 months, taking psychiatric medication for depression or anxiety and receiving psychotherapy for depression or anxiety and these associated with elevated anxiety: being female, recently on IV antibiotics and receiving psychotherapy [4]. Another study evaluating prevalence of symptoms of depression and anxiety reported in multiple linear regression analysis, only FEV1% predicted was independently associated with PHQ-9 depression scores, and no sociodemographic or clinical factors were associated with GAD-7 anxiety scores[17].

In our study, both depression (33.7% vs. 14.6%) and anxiety (21.8% vs. 8.5%) were much higher in mothers than fathers. Similarly, in a study among Italian population, mothers were more anxious than fathers (23.8% vs. 12.3%) and much more depressed than fathers (8.7% vs. 2.8%) [18]. The cultural similarities between these countries resulting in the mothers being the primary caregiver of CF patients and increased stress due to the caregiver burden might be the cause of higher depression and anxiety levels in mothers in both countries.

Although presence of chronic MRSA infection and recent hospital admission was associated with parental depression and anxiety, similar association was not found for pulmonary function test parameters. Catastini et al.[18] interpreted this as, the worsening of pulmonary function indicators (FEV1 and FVC) does not seem to affect the emotional state of the parents, who probably experienced the symbolic value of the worsening of the disease (use of therapies) more than the real clinical deterioration. In our study, chronic MRSA infection was associated with higher anxiety levels in mothers and the increased number of hospitalization and exacerbation in this group might be the possible causes.

Moreover, recent hospital admission was associated with increased depression in fathers. One possible reason might be the increased responsibilities on fathers during hospitalization (household tasks and care of other children etc.) because as mothers being the primary caregiver of CF patients in Turkey, most of the time they stay at the hospital during admission.

Smith et al, in contrast to our study, reported positive correlations between maternal depressive symptoms and adherence [19]. Our data revealed that maternal depressive symptoms associated with worse adherence to treatment. Physical and mental health of caregivers are critically important in the care of children with chronic illnesses. Mothers are the main caregiver of children with CF in our country and depression of the mothers may result in non-adherence to medications/airway clearance methods. Quittner et al.[20] also showed that caregiver depression was negatively associated with adherence to pancreatic enzyme use, with depressed caregivers demonstrating lower rates of adherence which resulted in changes in weight of patients.

To the best of our knowledge, before the TIDES study there was not any guidelines on screening of caregivers. ICMH recommended offering annual screening for depression and anxiety to at least one primary caregiver of children and adolescents with CF [9]. The problems related to treatment adherence might cause deterioration in patients' clinical status. This shows great importance of parental screening rather than only the children. Our findings support the possible positive outcomes of parental screening and intervention according to results.

The present study is the first study evaluating depression and anxiety in Turkish adolescent CF patients and parent caregivers by using the assessment tools recommended by CFF and ECFS.

This study has some limitations. One of the most important limitation of the study is the small sample

size. Secondly, socioeconomic determinants were not included in the study design which might be predictors of depression and anxiety. Adherence was not measured objectively, rather assessed by patient/parent self-reports. During the study period, the patients and parents with increased symptoms of anxiety and/or depression were referred to child psychiatrist. These patients were treated or followed up by the specialists according to the guidelines. We hope that these interventions would be helpful to increase psychological wellbeing and adherence to treatment protocol eventually.

In conclusion, symptoms of depression and anxiety are higher than normal population in both CF patients and their caregivers. Our study found that chronic MRSA infection and hospitalization in the last twelve months are associated with elevated psychological difficulties in parents of patients. Moreover, elevated depressive symptoms in mothers are negatively correlated with adherence to airway clearance in patients. Therefore, it is greatly important to screen the symptoms of depression/anxiety in both CF patients and their caregivers and intervene accordingly.

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