

# Identification of factors determining anxiety, depression and aggression, with particular emphasis on pain in Polish adolescents and young adults with cystic fibrosis

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**A** – Study Design, **B** – Data Collection, **C** – Statistical Analysis, **D** – Data Interpretation, **E** – Manuscript Preparation, **F** – Literature Search, **G** – Funds Collection

**Summary Background.** The prolonged survival of patients with cystic fibrosis leads to the search for predictors that determine their physical health and functioning in social and psycho-emotional areas, and allows for better understanding of the mutual interactions.

**Objectives.** The aim of the study was to assess the incidence of pain in patients with CF and clinical determinants of anxiety, depression and aggression.

**Material and methods.** The study covered 95 patients with CF aged 14–25 years. The analysis included: the intensity of pain (Numeric Rating Scale), the level of anxiety, depression and aggression (Hospital Anxiety and Depression Scale), the quality of sleep (Athens Insomnia Scale), FEV<sub>1</sub> and BMI.

**Results.** 42.1% ( $n = 40$ ) of patients with CF experienced pain, mainly moderate ( $n = 18$ ; 45%) and severe ( $n = 14$ ; 35%). In these patients, significantly higher median anxiety scores (6 vs 4) and median depression scores (3.5 vs 2) were recorded than in subjects without pain. Factors considerably determining anxiety scores were AIS scores ( $\beta = 0.56$ ) and sex ( $\beta = 0.22$ ), while depression scores were determined by AIS scores ( $\beta = 0.56$ ), BMI ( $\beta = -0.20$ ) and pain intensity ( $\beta = 0.20$ ). In turn, sex ( $\beta = 0.30$ ) and AIS scores ( $\beta = 0.19$ ) had an influence on aggression scores.

**Conclusions.** Pain occurs in a large proportion of patients with CF. Factors determining emotional disorders in patients with CF are pain, female sex, quality of sleep and body weight. Anxiety, depression and aggression have always been accompanied by poorer sleep quality.

**Key words:** sleep, depression, pain, anxiety, cystic fibrosis, adolescent, adult.

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## Background

Despite the fact that the development of medicine allows for better understanding and opens new pathways for the treatment of cystic fibrosis (CF), the condition continues to be a life-threatening disorder [1].

The prolonged survival of patients with CF leads to the search for predictors that determine their physical health and functioning in social and psycho-emotional areas, and allow for better understanding of the mutual interactions. The biological state of a patient with CF is already well understood and described [2], but the links between the biological state and other factors, for instance emotional, require further deepening of research.

Identified factors destabilizing the condition of a patient with CF include pain [3], sleep disorders [4] and negative emotions [5]. Pain is considered to be common in patients with CF, but its connotation and importance for the patient's functioning still appear to be underestimated. The pain problem in CF is sometimes ignored, and assumed to be an unspecific symptom. Clinical practice suggests that pain in this group of patients may accompany osteoporosis, spinal curvature, arthritis, sinusitis, emphysema and complications in the alimentary tract [6]. Also, physiotherapy may cause muscle tension that induces chest

and back pain, and conversely, intense dyspnea and cough may cause painful contractions of intercostal muscles [7]. Pain is a common problem in both children and adults with CF. It has negative clinical associations with life quality and the ability to successfully undertake treatment [3, 8].

Pain is also associated with depression, and depression may be a risk factor for the development of pain in patients with CF [9]. Negative emotions predispose patients towards higher perception of pain on one hand, but on the other hand, continuous pain, in its effects, may influence the incidence of negative emotions. Although epidemiological studies continue to provide data and information that could lead to a better understanding of the clinical manifestations of the disease, there are still many controversies regarding the importance of some risk factors, such as pain and depression in the pathogenesis of this disorder, and its management [10]. The findings emphasize the need to screen patients with CF for symptoms of depression and to treat co-morbid depression. There is an important need to continue to promote an integrated team approach to CF care, and to underline the need for multidisciplinary CF care teams to include a clinical psychologist.

Pain can lead to sleep disorders, which depend on the severity of the disease, the patient's sensitivity, previous treatments,



and the efficacy of analgesics. The combination of symptoms caused by the disorder and sleep problems produce deeper physical and mental discomfort, leading to disorganization of social and individual functioning [11]. Assessing the mutual interactions between anxiety, depression and aggression, with particular emphasis on pain and quality of sleep, is necessary, especially in adolescents and young adults with CF. Young people may not have fully developed skills of coping with the disease and therapy, and developmental tasks may make them particularly susceptible to emotional stress. Anxiety seems to be the basic background for emotional life, against which anger, annoyance, depression, lack of self-confidence, helplessness and the loss of control over the body appear.

## Objectives

The aim of the study was to assess the incidence of pain in patients with CF, and to examine the demographic and clinical determinants of anxiety, depression and aggression.

## Materials and methods

### Setting

The study comprised 95 subjects with CF, both sexes, aged 14–25 years, who reported to the follow up visit at the Institute of Tuberculosis and Lung Diseases in Rabka Zdroj.

The research was carried out between February 10, 2016 and February 28, 2017, and was approved by the Bioethics Commission of the Jagiellonian University in Krakow (No. 122.6120.275.2015).

### Participants

The inclusion criterion was stable state of health in the 4 weeks prior to enrolment (no worsening of clinical status, e.g. aggravation of dyspnea or cough, coughing up sputum, the use of assisted breathing or respiratory therapy). The study excluded patients who did not consent to participate in the study (the legal guardian's consent was necessary for patients under the age of 18), those after lung transplantation, or with mental or terminal diseases, and people who had traumatic experiences in the last 6 months (e.g. relationship breakdown, death of a significant person, job loss).

The level of pain intensity and pain relief were assessed using the Numeric Rating Scale, where 0 meant no pain/no pain relief, and 10 maximum pain/complete pain relief. The results of pain assessment were interpreted as: weak (1–3/10), moderate (4–6/10), and strong (over 6/10).

The Hospital Anxiety and Depression Scale (HADS), which was modified to assess the level of aggression and validated to Polish conditions, was used to evaluate anxiety and depression. In depression and anxiety subscales, the patient can obtain from 0 to 21 points (normal: 0–7 points, borderline: 8–10 points, clinical levels of symptoms  $\geq 11$  points); in the aggression subscale from 0 to 6 points (the higher the number of points, the higher the level of aggression).

The Polish version of the Athens Insomnia Scale (AIS) was used to assess the quality of sleep. If the symptom occurred at least three times a week during the last month, the patient assessed its severity on a scale of 1–3 points (0 was no symptom). A total score of at least 8/24 points may indicate insomnia.

A metric of our own design has been used to collect sociodemographic data and basic information about the patient's general state of health. Information on FEV<sub>1</sub> values over the last 4 weeks was obtained from patients' medical records.

## Statistical methods

Statistical analysis was performed using Statistica 12 software, including the "Medical Bundle" (StatSoft®, Poland). Intergroup differences for quantitative variables were verified using the *t*-student or Mann–Whitney test based on the distribution of variables, while  $\chi^2$  and Fisher's exact test were used for qualitative variables. Correlations between values of numerical parameters were determined on the basis of Spearman's (*R*) rank correlation coefficient.

A linear stepwise reverse regression was used to investigate demographic and clinical factors affecting anxiety, depression and aggression. The sum of points obtained in anxiety, depression and aggression subscales was a dependent variable. The logistic regression model was used to calculate the odds ratio for anxiety and depressive disorders depending on gender and the presence of insomnia. Statistical significance was assumed at  $p = 0.05$ .

## Results

### Participants and descriptive data

Statistical analysis was based on the results from 95 questionnaires that were completed mostly by male patients (56.8%), aged 17–25 years (73.7%). Patients who declared experiencing pain were assigned to the pain group (42.1%), while those who did not feel pain were assigned to the no pain group (57.9%). Demographic and clinical characteristics of patients are presented in Table 1.

**Table 1. Comparison of patients in terms of demographic and clinical characteristics based on reporting of pain**

Parameter		Pain ( <i>n</i> = 40)	No pain ( <i>n</i> = 55)	<i>p</i>
Age (years)	14–16	9 (22.5%)	16 (29.1%)	$\chi^2 = 0.577$ ; <i>p</i> = 0.749
	17–20	15 (37.5%)	20 (36.4%)	
	21–25	16 (40.0%)	19 (34.5%)	
Sex	Girls	20 (50.0%)	21 (38.2%)	$\chi^2 = 1.318$ ; <i>p</i> = 0.250
	Boys	20 (50.0%)	34 (61.8%)	
BMI (kg/m <sup>2</sup> )		19.6 ± 2.5	20.1 ± 3.1	<i>t</i> = -0.706; <i>p</i> = 0.481
FEV <sub>1</sub> (% of pred.)		68.6 ± 25.4	67.9 ± 20.7	<i>t</i> = -0.144; <i>p</i> = 0.885
Anxiety (scores)		6 (4–10)	4 (2–8)	<i>Z</i> = -1.994; <i>p</i> = 0.046
Depression (scores)		3.5 (2–7.5)	2 (1–6)	<i>Z</i> = -2.199; <i>p</i> = 0.027
Aggression (scores)		3.5 (2–4)	3 (2–4)	<i>Z</i> = -0.893; <i>p</i> = 0.371
AIS (scores)		6.5 (4–10)	5 (3–8)	<i>Z</i> = -1.239; <i>p</i> = 0.214
Co-morbidities*	yes	16 (40.0%)	29 (52.7%)	$\chi^2 = 1.504$ ; <i>p</i> = 0.219
	no	24 (60.0%)	26 (47.3%)	

Results presented as medians (interquartile ranges), mean (standard deviation) or numbers (percentages). Abbreviations: BMI – body mass index; FEV<sub>1</sub> – forced expiratory volume in 1 s; AIS – Athens Insomnia Scale, \* the co-morbidities included diabetes (*n* = 16), bronchial asthma (*n* = 15), nasal polyps (*n* = 10) and cholelithiasis (*n* = 8).

## Main results

### Prevalence of pain

In the pain group 8 patients (20%) suffered from mild, 18 from moderate (45%) and 14 from strong pain (35%).

The most common was pain of the abdomen (50%), head (47.5%) and chest (37.5%). Less frequently, pain was felt in the muscles (12.5%), spine (5%) and joints (5%). One source of pain was found in 35 (87.5%) patients, while in the remaining subjects it was located in several areas of the body. There was a moderate correlation between pain intensity and the number of pain sources ( $R = 0.44$ ;  $t = 3.081$ ;  $p = 0.003$ ).

Analgesic treatment was mainly based on the immediate administration of non-steroidal anti-inflammatory drugs and/or paracetamol and/or metamizol (70%). Patients took medications mainly after physical activity, when the pain intensity was  $\geq 3/10$  (mean pain relief after analgesic treatment was  $7.7 \pm 1.8$ ).

### The evaluation of the relationship between pain, emotional disorders and the quality of sleep

Patients with pain had significantly higher median anxiety scores and median depression scores than those without pain (Table 1). Pain intensity poorly correlates with anxiety scores ( $R = 0.25$ ;  $t = 2.498$ ;  $p = 0.014$ ) and depression scores ( $R = 0.27$ ;  $t = 2.277$ ;  $p = 0.006$ ).

There was no significant difference between patients from the pain and no pain groups in terms of aggression scores and AIS scores (Table 1).

### The evaluation of emotional disorder determinants

#### Anxiety

In the whole study group, anxiety disorders were diagnosed in 16 subjects (16.8%) and "borderline cases" in 17 (17.9%) patients with CF.

Factors determining anxiety scores were AIS scores and sex. This model explained 41% of anxiety scores variable variances (Table 2, model 1). If an insomnia variable was introduced into the regression model instead of AIS scores, then the model explained 31% of anxiety scores variable variances (Table 2, model 2).

Predictors	$\beta$	SE of $\beta$	$b$	SE of $b$	$t$	$p$
<b>Model 1. <math>R^2 = 0.41</math>; <math>F(2.92) = 33.040</math>; <math>p = 0.00</math></b>						
AIS scores	0.56	0.08	0.49	0.07	6.935	0.000
Sex <sup>Women</sup>	0.22	0.08	0.95	0.34	2.758	0.007
<b>Model 2. <math>R^2 = 0.31</math>; <math>F(2.92) = 21.635</math>; <math>p = 0.00</math></b>						
Insomnia	0.45	0.08	1.99	0.37	5.280	0.000
Sex <sup>Women</sup>	0.26	0.08	1.13	0.36	3.075	0.002

$\beta$  – standardized regression coefficient;  $b$  – non-standardized regression coefficient; SE – standard error;  $R^2$  – determination coefficient; AIS – Athens Insomnia Scale.

Median anxiety scores were significantly higher in patients with insomnia than in those with good quality of sleep (10 vs 4;  $Z = -4.549$ ;  $p = 0.000$ ), and in women than in men (7 vs 4,  $Z = 3.354$ ;  $p = 0.000$ ). The odds of anxiety disorders are 5.2 times higher in female patients with CF than in male patients (OR: 5.17; 95% CI: 1.52 to 17.53).

#### Depression

Depression was diagnosed in 6 patients (6.3%), and there were 12 "borderline cases" (12.6%) among subjects with CF. Depression scores strongly correlated with anxiety scores ( $R = 0.72$ ;  $t = 10.005$ ;  $p = 0.000$ ). Factors determining depression scores were: AIS scores, BMI and pain intensity. These variables explained 43% of depression scores variable variances (Table 3).

Table 3. Predictors of depression, the results of linear stepwise reverse regression ( $n = 95$ )

Predictors	$\beta$	SE of $\beta$	$b$	SE of $b$	$t$	$p$
AIS scores	0.56	0.08	0.42	0.061	6.933	0.000
BMI	-0.20	0.07	-0.27	0.104	-2.619	0.010
Pain intensity	0.20	0.08	0.23	0.097	2.435	0.016

$\beta$  – standardized regression coefficient;  $b$  – non-standardized regression coefficient; SE – standard error;  $R^2$  – determination coefficient; AIS – Athens Insomnia Scale;  $R^2 = 0.43$ ;  $F(3.91) = 22.560$ ;  $p = 0.000$ .

#### Aggression

Aggression scores were determined by sex and AIS scores. Gender and AIS scores explained 15% of aggression variable variances (Table 4). The level of aggression moderately correlated with the level of anxiety ( $R = 0.41$ ;  $t = 4.401$ ;  $p = 0.000$ ). Significantly higher levels of aggression were recorded in women than in men (Me: 4 vs 2.5;  $Z = 3.249$ ;  $p = 0.000$ ). The odds of a higher level of aggression in female patients with CF are 1.6 times greater than in male patients (OR: 1.6; 95% CI: 1.19 to 2.14).

Table 4. Predictors of aggression, the results of linear stepwise reverse regression ( $n = 95$ )

Predictors	$\beta$	SE of $\beta$	$b$	SE of $b$	$t$	$p$
Sex <sup>Women</sup>	0.30	0.09	0.47	0.15	3.066	0.002
AIS scores	0.19	0.09	0.06	0.03	1.994	0.049

$\beta$  – standardized regression coefficient;  $b$  – non-standardized regression coefficient; SE – standard error;  $R^2$  – determination coefficient; AIS – Athens Insomnia Scale;  $R^2 = 0.15$ ;  $F(2.92) = 8.254$ ;  $p = 0.000$ .

## Discussion

### Key results

Our study revealed that a significant proportion of CF adolescents and young adults experienced pain, as in the study conducted by Festini et al. [6]. Nearly 90% of the subjects indicated one source of pain, among which the digestive tract, head and respiratory system dominated. Lechnitz et al. [8] and Hayes et al. [12] obtained similar results in terms of pain location, whereas in the study conducted by Moraru et al. [10] nearly 34% of patients complained of various pain manifestations.

The study demonstrated a positive correlation between the level of pain intensity and the number of its source, but the correlation was moderate. Analgesia used by patients was primarily based on the immediate oral administration of paracetamol, metamizol and non-steroidal anti-inflammatory drugs. In the subjects' opinion, analgesic treatment brought considerable pain relief. The results could have been influenced by the stable state of the patient's health, but the effectiveness of analgesia could also result from good education about pain management by the medical team, especially nurses. Given the amount of time devoted to patients, nursing teams can use their professional competence to provide patients with information support for pharmacological and non-pharmacological methods of fighting pain and reducing anxiety [13].

The analysis of the material has confirmed the relationship between pain and higher levels of anxiety and depression. Similar results were obtained by Hayes et al. [12], proving that symptoms of depression and anxiety were more common among patients with pain. Importantly, the authors have demonstrated the association of pain not only with the greater risk of negative emotional states, but also with the higher probability of death.

The relationship between pain and aggression was not shown in our study. Higher levels of aggression have been re-

ported in female patients and those with sleep disorders. Higher levels of aggression also correlated with greater anxiety. It is difficult to compare the results because it was not possible to find studies based on the HADS scale extended by the part diagnosing aggression.

The problem of anxiety and depression is of particular importance among patients with CF due to the connotation with the patient's biological state. Being subjective experiences, anxiety and depression coexist with neurophysiological changes, and thus they can also somatise [14]. The studied emotions are also capable of mutual interactions, and by worsening the condition of a patient with CF they become determinants of his/her survival time [15, 16]. Duff et al. [17] demonstrated that feeling unwell was associated with increased depression scores, whereas Dantzer et al. [18] highlights the association between pathophysiological processes, such as inflammation, and increased depressive symptoms identified in the context of other medical conditions. The relationship between depression and anxiety was confirmed in our study results. The severity of anxiety and depressive symptoms was dependent on the quality of sleep. Matsuda and Tully [19] reported a relationship between poor quality of sleep and increased risk of depression and anxiety. In turn, Backström-Eriksson et al. [20] noted that females are more likely to suffer from anxiety disorders, as confirmed by our results.

Apart from the quality of sleep and anxiety, the level of depression was also affected by low BMI and pain intensity. There have been no reports on the association between BMI and depression in patients with CF. The literature mainly contains reports on the relationship between depression and overweight/obesity or anorexia [21, 22]. In patients with cystic fibrosis, BMI is a measure of physical well-being and good health control. Thus, a decrease in BMI can be perceived by the patient as a sign of deterioration of the health condition and, consequently, a shortening of survival time, becoming a factor destabilizing the psycho-emotional state.

The results of our study clearly indicate the relationship between pain, weight and sleep disorders, including insomnia, and the development of negative emotional states. This is of importance both for the patient and therapeutic teams

and institutions providing medical care. Mutual connotations between the study variables hinder the clinical assessment of the patient's condition and generate considerable costs for the treatment of these patients. At the same time, making a diagnosis of some negative emotional states can be difficult because of the wide range of symptoms, especially in young people [23]. Understanding the interactions between these variables is very important in the treatment process [24, 25] (both for nurses, physicians and patients).

## Why are the study results important?

The research tools are easy to use and can be applied by nursing teams and physicians. They serve for the examination of both young and adult patients, enabling us to objectify the results in different age groups. The examination of patients with risk factors, such as female gender, sleep disorders and pain is particularly indicated.

## The implications for clinical practice

The popularization of the need for screening in the study area can improve the well-being of patients and reduce the cost of treatment.

## Limitations of the study

The evaluation of anxiety and depression using only a screening tool, sleep assessment without objective tests (e.g. polysomnography), no control group, the lack of information on how often the subjects reported pain during the day, and the distinction between acute and chronic pain.

## Conclusions

Factors determining emotional disorders in patients with CF include female gender, the quality of sleep, pain intensity and BMI. Anxiety, depression and aggression are always accompanied by poor quality of sleep. The greater the pain intensity and the lower the BMI, the higher the severity of depressive symptoms in patients with CF.

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