



Prevalence of pain in adults with cystic fibrosis[☆]

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Abstract

Background: Cystic fibrosis (CF) may strongly condition the life of affected people. CF may be associated with relevant painful conditions caused by complications of the illness and also by therapy itself, which may represent an additional load of suffering. This study was aimed at evaluating the prevalence of pain symptoms in adult CF patients, if they are noticed and treated, and the influence of pain symptoms on patients' life. **Method:** Using a questionnaire, we examined 239 adults with CF (17% of the whole Italian adult CF population). **Results:** We found a high prevalence of painful episodes among CF adult patients, as for both intensity and frequency. In a 2 months period 32.6% of patients experienced episodes of pain described as intense to severe, and 29.7% had more than 10 occurrences of pain in the same location. Headache, gastric pain and backache were the most frequently reported kind of pain. 59.8% of subjects perceived pain episodes as the cause of unfavorable effects on their life. Only 42.6% of those with pain asked a CF center physician for help and another 3.5% a general practitioner. **Conclusion:** Painful symptoms can be the cause of a worsening of the quality of life for adults with CF; the relevance of pain in CF adult patients may often be underestimated; the assessment of pain should be routinely performed as a part of care in CF centers.

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1. Introduction

Life expectancy of people with cystic fibrosis (CF) has substantially increased over recent years. According to a recent study the life expectancy of a baby with CF born in 1990 is estimated at approximately 40 [1]. At the present time, a large number of CF patients are adults. In the United States, adults with CF represent 39.5% of the total and the predicted survival age is 33.4 years [2]. In Italy, approximately 38% of persons suffering from CF are over 18 [3].

The progressive deterioration in the health of patients who survive into adult life may cause a decline of their quality of life. In fact, because of their basic pulmonary

disease, they may be restricted in their work and social relations. Furthermore, the treatment necessary to keep the disease from advancing usually takes up a great deal of a CF adult's life, it is generally quite invasive and frequent hospitalizations are often necessary.

Besides these elements which negatively affect their quality of life, patients with CF frequently develop chronic complications due to their basic disease and, with growing frequency, to the treatment they undergo. In particular, among CF adults, there is a high prevalence of problems such as, *inter alia*, osteoporosis [4], hearing loss due to treatment with antibiotics [5], arthropathies [6], gastroesophageal reflux [7], fibrosing colonopathy [8], musculo-skeletal problems [9], female urinary incontinence [10] and vaginitis [11]. Many of these complications are accompanied by more or less marked pain symptoms, which go alongside other painful experiences due to the acute complications possible in CF, such as pneumothorax and distal intestinal obstruction

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Table 1
Questions and possible answers in the administered questionnaire

Question	Possible replies
1 In the past 2 months, have you experienced one or more of the following painful symptoms?	<ul style="list-style-type: none"> – Headache or pain in the frontal region – Cervical pain – Pain in one or more joints – Backache or lumbar pain – Painful bones or muscular pain – Pain in the stomach, heartburn – Abdominal pain – Chest pain – Other types of pain not listed (please specify)
2 For each case in which the reply to question 1 was yes, what was the maximum intensity of pain, on a rating scale of 1 to 10?	Numeric rating scale 1 to 10: (1 mild, 4 moderate, 7 strong, 10 severe)
3 For each case in which the reply to question 1 was yes, how many painful episodes did you experience during the time period considered?	<ul style="list-style-type: none"> – 1 – from 2 to 5 – from 6 to 10 – more than 10
4 What did you do to fight the pain? Only one reply is allowed.	<ul style="list-style-type: none"> – I consulted a doctor at the CF center. – I consulted my GP. – I consulted relations and friends. – I made my own decision on how to fight the pain. – I did nothing to fight the pain.
5 If you adopted any remedies, what were they? One or more replies are allowed.	<ul style="list-style-type: none"> – I took drugs. – I took homeopathic products. – I adopted non-pharmacological remedies. (please describe)
6 If in question 1 you reported experiencing pain, did the pain give rise to one or more of the following negative consequences?	<ul style="list-style-type: none"> – I felt restricted in carrying out my normal everyday activities. – I was unable to carry out my normal everyday activities. – I lost days at work, school or studying. – I suffered from sleeping disorders. – I did not keep to the prescribed treatment.

syndrome (DIOS), and the numerous invasive practices suffered by patients as, for example, frequent venipunctures for the administration of antibiotics.

In clinical practice, nurses at Italian CF centers noticed that an increasing number of adult CF patients complained of pain. This made us realize that the problem of pain in adult CF patients was worth assessment from an epidemiological point of view, with particular regard to the consequences it had on the patients' quality of life.

Until now, pain in CF adults has received little attention in literature, since only a few authors have studied the relevance of pain in CF. Some have dealt with pain in the terminal stages of CF, and have included children and adolescents in their studies [12]. So far only a few, limited data are available on the prevalence of the problem outside the terminal stages of the disease and on its consequences on patients' everyday life. In particular, the problem of pain in CF adults has received only limited attention, and has been analyzed only in very small groups [13–15].

The objectives of our study were:

To evaluate the prevalence of pain symptoms in adults with CF.

To evaluate if and to what extent pain in CF patients is detected and treated.

To evaluate the impact of pain on the daily life of CF adults.

2. Materials, subjects and methods

The study was devised and conducted by the Italian Group of Cystic Fibrosis Nurses. It commenced in March 2001 and ended in June 2001.

To collect data we used a standard questionnaire setting out six questions aimed at discovering the location of painful symptoms, their frequency and intensity, how they are treated and their effects on every day life. Table 1 illustrates the questions on the questionnaire. The questions put to patients referred to pain experienced in the 2 months prior to completion of the questionnaire.

The questionnaire was administered to people affected by CF aged 18 or more who were followed in one of

the Italian CF centers. Subjects to be examined were chosen randomly by each center participating in the study, by drawing among all the adult patients who were visited at the center in the study period. The proportion of subjects drawn in each center was equal to the proportion of CF adults followed by that center with regard to the total number of Italian CF adults.

The questionnaires were administered during programmed routine visits to the center. A nurse of the CF center obtained the patients' consent and explained the meaning of the questions. Each patient answered the questionnaire with no limits of time and with the possibility to ask the nurse for explanations about the questions, if unclear. The nurse who administered the questionnaire filled out a record with the following clinical data of each patient: body mass index (BMI), forced expiratory volume at 1 s (FEV1), the presence of pancreatic insufficiency, the presence and the type of chronic lung colonization by respiratory pathogens. All 24 Italian CF centers and CF units in which adult patients were followed, were invited to participate.

The collected data were stored in a computerized database and were processed with the Epi info 2002, rev.1 program, by World Health Organization. Absolute and relative frequencies of the observed variables were calculated together with the 95% confidence intervals (95% CI) of the relative frequencies.

3. Results

Fifteen Italian CF centers out of 24 participated to the study. Two hundred and fifty adult CF patients were invited to participate (128 females, 122 males). Two hundred and thirty-nine CF patients accepted to answer the questionnaire. On the basis of the data of the Italian CF registry [3] they represent 17% of the whole Italian adult CF population. Among those examined, 125 were females (52.3%) and 114 males (47.7%). Mean age was 26.1 years (median 25 years, range 18–43). Males' mean age was 26.3 years (median 25 years—min. 18 max. 42). As for females, mean age was 25.78 years (median 25 years, range 18–43)

3.1. Clinical conditions of the examined patients

Mean BMI of males was 20.97 (± 2.88 S.D., median 20.84). Mean BMI of females was 19.93 (± 2.39 S.D., median 19.94). Mean FEV1 was 56.71% of the predicted (± 23.33 S.D., median 52%). 71.9% of patients had pancreatic insufficiency. Chronic *Pseudomonas aeruginosa* colonization of lungs was present in 71.9% of patients, whereas 10.04% were chronically colonized by *Burkholderia Cepacia*.

3.2. Prevalence of painful symptoms in CF adults

225 patients (94.1%, 95% CI:90.4–96.4) reported they had episodes of pain during the previous 2 months.

Table 2

Absolute frequencies (*n*), percentages (%) and 95% confidence intervals of percentages (95% CI), of the different locations and types of pain reported; Absolute frequencies, percentages and 95% confidence intervals of percentages, of the highest intensity of pain experienced by each patient; Absolute frequencies, percentages and 95% confidence intervals of percentages, of frequencies of pain reported by each patient in the 2-months period; Percentages are calculated on the total of the examined group

	<i>n</i>	%	95% CI
Location/type of reported pain			
Headache or pain in the frontal region	151	63.1	56.9–69.0
Pain in the stomach, heartburn	123	51.4	45.1–57.7
Backache or lumbar pain	115	48.1	41.8–54.4
Painful bones or muscular pain	106	44.3	38.1–50.6
Pain in one or more joints	99	41.4	35.3–47.7
Abdominal pain	79	33.0	27.4–39.2
Chest pain	76	31.8	26.2–37.9
Cervical pain	68	28.4	23.1–34.4
Other types of pain not listed	14	5.8	3.5–9.5
Highest intensity of pain experienced by each patient			
no pain	14	5.8	3.5–9.5
from 1 to 3	48	20.1	15.5–25.6
from 4 to 7	99	41.4	35.3–47.7
from 8 to 10	78	32.6	27.0–38.8
Frequency of pain episodes for each patient in the 2-month period			
no pain	14	5.8	3.5–9.5
once	32	13.4	9.6–18.2
twice to five times	74	30.9	25.4–37.1
6 to 10 times	48	20.1	15.5–25.6
more than 10 times	71	29.7	24.2–35.7

3.3. Location and type of pain

Table 2 shows the type and/or the location of the pain symptoms reported by CF adults in the considered period, ordered from the most to the least reported. Percentages are calculated on the total of the examined group and are not reciprocally exclusive because many patients reported the presence of more than one pain symptom at the same time. Among the types or locations of pain not listed in the questionnaire but reported by patients as 'Other', the most reported were the pain caused by oral and genital mycosis and by renal colics.

It is noticeable that 38.4% of subjects (*n*=92) reported painful episodes in four or more different locations over the 2-months period, and 16.8% (*n*=40) in three locations at the same time.

37.2% of patients (*n*=89) reported they had both headache and backache in the period and 34.7% (*n*=83) reported both headache and gastric pain.

3.4. Intensity of pain

Table 2 shows the highest intensity of pain experienced by each patient in the considered period. 10.8% of CF adults (*n*=26, 95% CI:7.5–15.4%) rated 10 as their most intense pain, that is 'severe'.

Table 3

Percentages (%) and 95% confidence intervals of percentages (95% CI), of severe pain and of pain more recurrent than 10 times in the period, among the patients who complained for each type of pain. Percentages are calculated on the number of patients who complained for each type of pain

	Severe pain		Pain which occurred > 10 times	
	%	95% CI	%	95% CI
Headache or pain in the frontal region	6.6	3.6–11.7	14.6	9.8–21.0
Backache or lumbar pain	8.7	4.7–15.2	17.4	11.5–25.3
Pain in the stomach, heartburn	2.4	0.8–6.9	14.6	9.4–21.9
Pain in one or more joints	4.0	1.5–9.9	18.1	11.8–26.9
Painful bones or muscular pain	3.7	1.4–9.3	11.3	6.6–18.7
Chest pain	2.6	0.7–9.1	13.3	7.3–22.5
Abdominal pain	2.5	0.7–8.7	11.4	6.1–20.2
Cervical pain	4.4	1.5–12.1	10.3	5.0–19.7
Other types of pain not listed	7.1	1.2–31.4	7.1	1.2–31.4

3.5. Frequency of pain

Table 2 shows the frequencies of episodes of pain reported by each patient for at least one type of pain in the 2 previous months.

3.6. Prevalence of severe pain and of recurrent pain, according to the location or type of pain

Table 3 shows, for each location or type of pain, the percentages of severe pain (i.e. rated 10) and of pain that occurred more than 10 times in the considered period.

In our group of patients, backache is the type of pain most frequently present in severe form, whereas joint pain is the type of pain that occurs in the most recurrent form.

3.7. What patients did to fight pain

Among the 225 patients who reported pain symptoms, 59 (26.2%, 95% CI:20.9–32.2) did nothing to fight the pain. Fifteen patients (6.6%, 95% CI:4.1–10.7) decided on their own what kind of measures to take and 47 (20.8%, 95% CI:16.1–26.6) consulted relatives and friends. Ninety-six subjects (42.6%, 95% CI:36.3–49.2) asked a CF center physician for help whereas 8 (3.5%, 95% CI:1.8–6.8) consulted their general practitioner.

Table 4

Absolute frequencies (*n*), percentages (%) and 95% confidence intervals of percentages (95% CI), of negative consequences of pain on day-to-day life, among patients who had pain. Percentages are not reciprocally exclusive

	<i>n</i>	%	95% CI
Restriction in carrying out normal everyday activities	90	40	33.8–46.5
Inability to carry out normal everyday activities	36	16	11.7–21.3
Lost of days at work, school or studying	50	22.2	17.2–28.1
Sleeping disorders	68	30.2	24.6–36.5
Failure to perform the prescribed treatments	25	11.1	7.6–15.8

3.8. Remedies adopted

Among the 166 patients who decided to fight pain, 152 (91.5%, 95% CI:86.3–94.9) took drugs, 3 (1.8%, 95% CI:0.6–5.1) took homeopathic products and 37 (22.2%, 95% CI:16.6–29.2) adopted non-pharmacological remedies. Percentages are not reciprocally exclusive. Among the non-pharmacological remedies adopted patients reported massages, acupuncture, herbal remedies, physical activity and rest.

3.9. Consequences of pain on daily life

Among the 225 patients who suffered from pain episodes, 143 (63.5%, 95% CI:57.1–69.5) reported that pain caused unfavorable effects on their day-to-day life. Table 4 shows the negative consequences of pain on daily life reported by patients. Since more answers were possible, percentages are not reciprocally exclusive. Patients who reported one or more negative effects of pain on their daily life represent 59.8% of the whole examined group of adults with CF.

4. Discussion

Our study examined for the first time the prevalence of pain in a large group of adults suffering from CF. It showed that in a group of Italian adults with CF, representing one sixth of the entire adult CF population, there is a high prevalence of pain, with regard to both

intensity and frequency; almost one third of the patients examined complained of pain described as strong to severe, 11% reported severe pain. Almost one third of patients complained of more than 10 episodes of the same type of pain during the period considered.

There are many conditions and complications in CF that may give rise to pain symptoms, even outside acute situations like pneumothorax and pulmonary exacerbations. Our study revealed that headache and gastric pain are widespread among adults with CF. Backache is also common and is the type of pain most frequently present in severe form. Joint pain is the type of pain that occurs in the most recurrent form.

Headache and frontal pain may accompany chronic sinusitis and nasal polyps, which are frequent in CF [16]. In more advanced stages of the disease, headache may be the consequence of hypercarbia and/or hypoxia.

With regard to gastric pain, gastro-oesophageal reflux is a frequently encountered complication in CF and it is probable that the cause of some of the pain which our patients defined as heartburn may be related to it.

With regard to backache, some papers report an increased prevalence of excessive kyphosis in patients with CF [9] as well as postural abnormalities and vertebral wedging [17], which could explain this symptom.

CF related arthritis is a frequently described condition in CF, which occurs with joint pains. When more serious pulmonary conditions are involved, another form of joint disease described in CF adults is the hypertrophic pulmonary osteoarthropathy, which occurs with joint pains and has an insidious onset [18].

Osteoporosis occurs with increasing frequency in patients with CF [4] and may be the cause of bone pains and severe back pains.

DIOS and fibrosing colonopathy, which have also been reported in adults with CF, are conditions associated with painful abdominal symptomatology in CF. Among the possible causes of abdominal pain is also Chron's disease, whose incidence is 17 times higher in persons with CF than in the general population [8].

However, even the treatment of CF itself may be cause of painful symptoms. The location and high prevalence of some types of pain observed in our study would appear to confirm this possibility. It has been suggested that among the possible iatrogenic causes of pain in CF adults respiratory physiotherapy may play a role and is indicated as the possible origin of chest and back pain [19]. Prolonged oxygen therapy may be the cause of headache, following dryness and flogosis of the paranasal sinuses. In addition, a high incidence of antibiotic related genital candidosis has been reported [11]. It is known that among drugs, the frequent use of NSAIDs and cortisone drugs is the possible cause of gastralgia, while the use of fluoroquinolones, which is frequent in CF patients, has occasionally been associated

with the onset of arthralgia [20]. High doses of pancreatic enzymes have been correlated to the onset of fibrosing colonopathy [8]. Even though transitory, the pain caused by the administration of i.v. Pamidronate, used in the treatment of osteoporosis, has been reported [21].

It must be emphasized that our study did not investigate pain caused by the procedures to which CF adults are subjected. For example, they undergo frequent venipunctures necessary for taking blood samples and administering cycles of i.v. antibiotic treatment. These and other invasive procedures are a considerable burden for CF adults. Our questionnaire did not contemplate procedural pain among the possible types of pain to report. From this point of view, our work may well have underestimated the overall weight of pain on these patients.

Thanks to an extended survival rate, most CF sufferers now survive into adult life and, like their peers, have to face the problems of their school career, earning their living, placement in the work environment and long-term planning of their family and social life. In facing their adult life commitments, the disease represents a heavy burden for these people. In many circumstances, it stops them from undertaking normal activities. Our study has revealed that pain may represent a cause of suffering and difficulty, which accompanies and adds to those caused by their basic pathology. In fact, almost 60% of the CF adults we studied reported that the painful symptomatology stopped or restricted their normal daily activities.

The negative effects of pain (as for example, sleeping problems) reported by the patients regard not only their social activities but also their individual well-being, and may even have repercussions on their very state of health, since they can be the cause of abandoning treatment.

Chastain report that in a group of 31 CF adults, 64% complained that pain interfered significantly with their daily lives [14]. Bilton et al. reported a percentage of 63% in a sample of 66 adults [13].

One particularly interesting fact emerging from our study is that only just over half the patients complaining of pain turned to their doctor for help. The paper by Bilton, on the contrary, reports a higher figure [13], while Eksterowicz, although not supplying data, acknowledges the possibility that pain in CF patients is frequently underestimated [22].

This goes hand in hand with another particularly important fact, i.e. more than a quarter of CF adults, did nothing to alleviate their pain and simply endured it.

In our opinion, these two facts may imply that there are potential difficulties and obstacles to effectively face the problem of pain in CF adults. In this connection, two considerations can be made. From the patient's

point of view, our data appear to suggest that CF adults tend to endure their pain without reporting it.

If the data are considered from the point of view of the caregivers' responsibility, we can hypothesize that there is a problem of caregivers recognizing and paying attention to the patient's pain, i.e. pain may be not recorded or perceived as an aspect of the patient's clinical condition that influences his quality of life or his clinical condition.

One of the effects we aim to produce with the results of our study is to awaken caregivers of CF patients to the importance of pain in these patients. The data we have recorded draw attention to the necessity for a routine evaluation of CF patients' pain, making it an integral part of periodic controls and clinical assessment. Furthermore, they emphasize the need for caregivers to set themselves the target of treating pain in adults so that they can, as far as possible, relieve this burden on their patients' already difficult daily lives.

The relief of pain in CF patients must therefore be approached from two directions: on the one side, pain relieving treatment should aim at treating painful symptoms directly related to the basic pathology or to related complications or clinical manifestations, the onset of which is sometimes insidious and with a tendency to become chronic. On the other, it should be directed at reducing the painful effects of essential drugs and treatment.

One of the obstacles to the pharmacological treatment of pain in these patients is represented by the side effects of some drugs, as for example, constipation caused by opiates, which may favor the onset of DIOS. In some patients, hepatic damage caused by the disease and renal overload, to which many patients are subject due to the high doses of antibiotics and drugs taken every day, may be considered a limitation to the use of some pain-killing drugs. In many painful conditions, non-pharmacological techniques, such as deep breathing, relaxation, imagery, distraction, calming self-statements, heat, cold, massage and exercise may be effective [23].

The questionnaire used for our study probably lacked the capacity to record some types of pain: it did not, in fact, contemplate pain in the genital area or the oral cavity. The patients themselves, however, indicated painful areas that were not envisaged, by using the open option in one of the questions.

In conclusion, our study revealed a high prevalence of pain in a large group of adults suffering from cystic fibrosis. It also showed that pain negatively affects the daily lives of over half the patients examined, often quite significantly, and in such a way as to restrict their daily activities. It also brought to light that in more than half the cases CF patients do not report pain to their caregivers and in a quarter of cases pain is simply endured.

With the progressive increase of the average survival age of CF patients, the problem of managing pain in these patients is destined to assume increasing importance and should be carefully assessed and dealt with.

The assessment of pain should become a routine procedure in CF clinical examination and attention to pain-related problems should become an integral part of care in CF centers.

A pain management specialist should be included on the staff of CF centers or should be among the professionals to whom the center can refer on a routine basis.

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