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Urinary Incontinence and Quality of Life in Women with Cystic Fibrosis

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Abstract

Context: Stress Urinary Incontinence (SUI) is recognized as a common complication in women with CF.

Objective: The primary objective of this study was to verify the prevalence of Urinary Incontinence (UI) and its associations with Quality of Life (QoL) in adult women with CF; secondarily, its associations with cough score, nutritional aspects and pulmonary function.

Design: cross-sectional study. **Patients:** female patients aged 18 years and older. **Interventions and main outcome measure:** The patients answered the international consultation on incontinence questionnaire short form, the Kings Health Questionnaire, and the Leicester Cough Questionnaire. Nutritional assessment was obtained. Sputum bacteriology and lung function were also performed.

Results: Fifty-two women were included, with mean age of 29.0 ± 9.7 years and mean forced expiratory volume in one second (FEV 1) (% of predicted) of 50.1 ± 21.7%. Thirty-two patients (61.5%) presented symptoms of UI, 23 (44.2%) of stress UI and 9 (17.3%) of mixed UI. However, there was no significant association between UI and pulmonary function, sputum bacteriology, and cough score ($p>0.05$). There was a significant association between UI and QoL variables ($p<0.05$).

Conclusion: this study identified a prevalence of 61.5% of UI in women with CF. The presence of UI resulted in a negative impact on QoL in women with CF.

Keywords: Cystic fibrosis; Urinary incontinence; Pulmonary function; Quality of life; Cough

Introduction

Cystic Fibrosis (CF) is an autosomal recessive genetic disorder associated with elevated levels of sweat electrolytes, exocrine pancreatic insufficiency, and chronic respiratory infections [1]. The disease is caused by mutations in a gene located on the long arm of chromosome 7 that encodes the Cystic Fibrosis Transmembrane Regulator (CFTR) protein. Pathophysiology involves the absence of activity or partial functioning of the chlorine channels. Change in conductance of this channel promotes an electrolyte imbalance leaving the extracellular surface dehydrated. In the lungs, increased extracellular viscosity leads to mucociliary transport impairment, mucus obstruction, inflammation, and recurrent respiratory infections [2]. Cough is one of the most common symptoms in this population, with an average prevalence of 94% [3].

Advances in therapies and treatments resulted in a significant increase in life expectancy and extra pulmonary conditions become more frequent such as Urinary Incontinence (UI) [4]. The International Continence Society considers UI as any involuntary loss of urine. It also classifies as Stress Urinary Incontinence (SUI) the loss of urine concomitant with physical exertion such as jumping, coughing, sneezing; Urgency Urinary Incontinence (UUI) such as loss of urine proceeded by urinary urgency; and Mixed Urinary Incontinence (MUI) - loss of urine in the two previous situations [5].

SUI is recognized as a common complication in women with CF, presenting a prevalence of 30% to 69% [6,7]. And has a negative impact on the performance of respiratory physiotherapy [8] UI is a condition that dramatically affects quality of life (QoL), compromising physical, emotional, psychological and social well-being and can affect individuals of all ages, both sexes and all social and economic levels [9].

A systematic review [4] synthesized published articles investigating the prevalence, severity and impact of UI associated with CF. Twelve studies met selection criteria. The prevalence ranged from 5% to 76%. Age and gender contributed to this variability. Worry and embarrassment were features for many; others were less affected. This review concluded that the prevalence, characteristics and impact are poorly understood, which is made worse by inconsistent definitions across studies. Future research, using a standardized definition of UI inclusive of

prevalence, severity and patient burden, is required to further understand the impact of UI in both sexes.

Also, due to the heterogeneity of the disease, the survival effects observed in studies of adult samples, and the presence of variability between populations, there is a clear need to seek further information regarding the prevalence of UI and its impact in QoL in different cohorts of patients with CF. So, the main objective of this study was to verify the prevalence of UI and its associations with QoL; secondarily, to verify its associations with cough score, nutritional aspects and pulmonary function in adult women with CF.

Materials and Methods

Study outline

This cross-sectional study was carried out with prospective data collection. The study was conducted in the Adult CF Program of Hospital de Clínicas de Porto Alegre (HCPA), Porto Alegre, and southern Brazil. The research protocol was approved by the Ethics and Research Committee of HCPA with protocol number 65415217.7.0000.5327 and all study participants signed the Informed Consent Form. This study was conducted in accordance with the Declaration of Helsinki.

Study population

A total of 52 women with CF were sequentially screened during outpatient appointment between January and December 2018. There was no refusal to participate in the study. The study included female patients aged 18 years or older, regularly followed up in the Adolescents and Adults CF Program, with a diagnosis of CF confirmed by clinical history, altered sweat test (chlorine greater than 60 mmol/L) in at least two samples and/or molecular genetic study showing two mutations known to cause CF. All patients should be clinically stable, defined as no recent change (in the last 30 days) in medication, with at least 30 days since completion of last intravenous or oral antibiotics for pulmonary exacerbation.

Exclusion criteria were the presence of neurological disorders, pregnancy, and cognitive inability to answer the questionnaires and previous surgery for IU.

Measures and instruments

The questionnaires were self-administered and were answered by individuals at the end of the outpatient appointment in a research room. The International Consultation on Incontinence Questionnaire Short Form (ICIQ-SF) assesses the impact of UI on QoL and the qualification of women's urinary loss. It consists of 4 questions that assess the frequency, severity, and impact of UI [10] these 4 questions add up to a number of points that determine whether the impact is absent (0 points), if the impact is mild (1 to 3 points), if the impact is moderate (4 to 6 points), if the impact is severe (7 to 9 points) and if the impact is very severe (10 or more points) [11].

The Kings Health Questionnaire (KHQ) assesses QoL and consists of 30 questions divided into 9 domains: health perception, UI impact, task limitation, physical limitation, social limitation, personal relationships, emotions, sleep/energy, and measures of gravity. The KHQ is punctuated by each of its domains; the scores vary from 0 to 100 and the higher the score obtained, the worse the QoL related to that domain. There is also a scale of symptoms that consists of the following items: urinary frequency, nocturia, urgency, bladder hyperreflexia, SUI, nocturnal enuresis, sexual intercourse incontinence, urinary infections and bladder pain [9].

The impact of chronic cough on QoL was evaluated by applying the Leicester Cough Questionnaire (LCQ) [11]. It consists of 19 items subdivided into three domains: physical (questions 1,2,3,9,10,11,14 and 15), psychological (questions 4,5,6,12,13,16 and 17) and social questions 7,8,18 and 19). Responses are scored by the patient on a Likert scale ranging from 1 to 7 points. For the calculation of the LCQ, a sum of the scores of the questions of each domain must be made. This value is divided by the number of questions in the respective domain. The total score is the result of adding the scores of each domain and ranges from 3 to 21, and a score closer to 21 indicates a better health status or a lower cough influence on the patient's QoL.

Sputum microbiology was evaluated as an indirect marker of pulmonary disease severity [12]. The bacteria identified in the last three bacteriological sputum examinations performed at HCPA were registered. Bacteriological examinations of sputum were performed at the HCPA microbiology service. The routine outpatient bacteriological evaluation of sputum involves the collection of a sample at each visit (usually every 60 days) or at each hospital stay.

Pulmonary function tests were performed using a computerized spirometer (Jaeger-v 4.31, Jaeger, Wuerzburg, Germany). Forced Vital Capacity (FVC), forced expiratory volume in the first second (FEV 1), and FEV 1/FVC ratio in liters and % predicted were recorded. Patients were classified according to Brazilian guidelines for pulmonary function tests [13].

The nutritional risk assessment was obtained by calculating the Body Mass Index (BMI) by applying the formula that divides the value of the current weight (kg) by the square of the height (meters)-BMI=weight/height [2,13].

Additional information about previous UI surgery and prolapse bladder was also obtained through review of the patients' medical records [14].

Statistical analysis

Quantitative data are presented as mean ± Standard Deviation (SD) or as median (Interquartile Range-IQR). Qualitative data are expressed in n (% of all cases). Initially, patients were divided into two groups, according to the presence or absence of UI. Continuous variables with normal distribution were analyzed by the t-test for independent samples and continuous data without normal distribution or ordinal data were analyzed by the Mann-Whitney U-test. Qualitative data were analyzed using the chi-square test, using, when necessary, Yates correction or Fisher's exact test, using standardized residuals adjusted to locate the difference.

Multivariable analyses were performed by using logistic regression techniques with enter method. The Odds ratio (OR) from this analysis should be the OR for UI. Selected variables with a P<0.10 should be introduced in the binary logistic regression, controlled by age.

Data were analyzed using the Statistical Package for the Social Sciences, version 20.0 (SPSS Inc., Chicago, IL, USA). The level of statistical significance was set at p<0.05. All reported probabilities were two-tailed.

Sample Calculation

The calculation of the sample size was estimated from the study of Reichman G. et al. 2016 [15]. For purposes of descriptive statistical analysis, the sample size estimation was performed using the dichotomous variable presence of urinary incontinence. For a ratio of 0.30, 95% confidence level and a total range of the confidence interval of 0.25, a total of 52 patients are required.

Results

Between January and December 2018, 52 women attended the adult CF outpatient clinic. All of them agreed to participate in the study. None of them had previous UI surgery or prolapse bladder. So, the study included 52 women with CF, with mean age of 29.0 ± 9.7 years, BMI 20.7 ± 2.5, FEV 1 (% of predicted) 50.1 ± 21.7%. Thirty-two (61.5%) presented symptoms of UI, 23 (44.2%) SUI and 9 (17.3%) MUI. Table 1 describes the general characteristics of the sample studied.

Table 1: General characteristics of women with CF included in the study.

Variable	n=52
Age (years), mean ± SD	29.0 ± 9.7
Age of CF diagnosis (years), median (IQR)	11 (1.6-19.8)
BMI (Kg/m²), mean ± SD	20.7 ± 2.5
CF related diabetes, n (%)	8 (15.4)
Pancreatic insufficiet, n (%)	42 (80.8)
FVC (L), mean ± SD	2.3 ± 0.9
FVC (%), mean ± SD	63.5 ± 20.2
FEV 1 (L), mean ± SD	1.6 ± 0.8
FEV 1 (%), mean ± SD	63.2 ± 21.9
FEV 1/FVC(%), mean ± SD	50.1 ± 21.7
UI, n (%)	32 (61.5)
SUI, n (%)	23 (44.2)
MUI, n (%)	9 (17.3)

CF=cystic fibrosis, n=number of cases, SD=standard deviation, IQR=interquartile range, BMI=body mass index, FVC=forced vital capacity, FEV 1=forced expiratory volume in the first second, UI=urinary incontinence, SUI=stress urinary incontinence, MUI=mixed urinary incontinence.

Table 2 classifies patients in two groups according with presence or absence of UI. There was no significant association between the presence of UI and sputum bacteriology, BMI, pulmonary function and QoL related to cough (p>0.05) among the groups with and without UI. There was significant association between UI and KHQ QoL variables in the domains of health perception (p=0.030), personal life (p<0.001), task limitation (p<0.001), physical limitations (p=0.043), social limitations (p=0.001), personal relationships (p<0.001), emotions (p<0.007), sleep (p=0.039) and severity (p=0.001) between groups.

Table 2: Demographic, pulmonary function and quality of life variables according to the urinary incontinence classification.

P value	Without UI	UI	Variable
	n=20	n=32	
0.466	27.7 ± 9.9	29.8 ± 9.9	Age (years), mean ± SD
0.745	11 (1.6-17.8)	11 (0.8-21.5)	Age of CF diagnosis (years), median (IQR)
0.637	20.6 ± 2.4	20.9 ± 2.6	BMI (Kg/m²), mean ± SD
			Sputum bacteriology
0.249	15 (28.8)	19 (36.5)	MSSA, n (%)
0.565	1 (1.9)	3 (5.8)	MRSA, n (%)
0.519	12 (23.1)	22 (42.3)	Pseudomonas aeruginosa, n (%)
0.728	3 (5.8)	6 (11.5)	Burkholderia cepacia, n (%)
			Spirometry
0.708	2.4 ± 0.9	2.3 ± 0.8	FVC (L), mean ± SD
0.912	62.3 ± 25	63.5 ± 20.2	FVC (%), mean ± SD
0.453	1.7 ± 0.9	1.5 ± 0.7	FEV 1 (L), mean ± SD
0.569	62.3 ± 25	63.5 ± 20.2	FEV 1 (%), mean ± SD
0.136	71.2 ± 12	65.9 ± 12.3	FEV 1/FVC, mean ± SD
0.159	82.0 ± 13.1	76.4 ± 14.3	FEV 1/FVC (%), mean ± SD
			LCQ domains score (points)
0.465	5.3 ± 1.4	5.5 ± 1.3	Physical, mean ± SD
0.48	5.2 ± 1.8	5.5 ± 1.2	Psychological, mean ± SD

0.387	6.0 ± 1.5	6.3 ± 1.1	Social, mean ± SD
0.33	16.5 ± 4.2	17.3 ± 3.0	Total, mean ± SD
			KHQ domains score, (points)
0.03	36.3 ± 12.8	47.7 ± 20.4	General health perception, mean ± SD
<0.001	0 (0-0)	66 (33-66)	Impact of UI, median (IQR)
<0.001	0 (0-0)	16 (0-33)	Task limitations, median (IQR)
0.043	0 (0-0)	0 (0-16)	Physical limitations, median (IQR)
0.001	0 (0-11)	11 (11-11)	Social limitations, median (IQR)
<0.001	0 (0-0)	33 (24.5-33)	Personal relationships, median (IQR)
0.007	0 (0-0)	0 (0-19.5)	Emotions, median (IQR)
0.039	0 (0-0)	0 (0-12)	Sleep/Energy, median (IQR)
<0.001	0 (0-0)	25 (2-45.8)	Severity measures, median (IQR)

CF=Cystic Fibrosis, UI=Urinary Incontinence, n=number of cases, SD=Standard Deviation, IQR=Interquartile Range, BMI=Body Mass Index, MSSA=Methicillin Susceptible Staphylococcus Aureus, MRSA=Methicillin-Resistant Staphylococcus Aureus, CVF=Capacidade Vital Forçada, VEF 1=Volume Expiratório Forçado no primeiro segundo, FVC=Forced Vital Capacity, FEV 1=forced expiratory volume in the first second, LCQ=Leicester Cough Questionnaire, KHQ=Kings Health Questionnaire.

Table 3 shows the subgroup of incontinent CF women and how much symptoms affected their lives.

Table 3: KHQ questionnaire: women with CF answered to how much the symptoms of UI affect their life

A lot	6 (18.4)
Urgency, n (%)	10 (28.1)
A little	2 (6.2)
Moderately	3 (9.4)
A lot	4 (12.5)
Urge incontinence, n (%)	10 (28.2)
Moderately	9 (28.2)
Stress incontinence, n (%)	23 (71.9)
A little	20 (62.5)
Moderately	2 (6.3)
A lot	1 (3.1)

KHQ=Kings Health Questionnaire, CF=Cystic Fibrosis, n=number of cases, UI=Urinary Incontinence.

Table 4 shows the impact of QoL by ICIQ-SF. Forty one percent of incontinent women scored 10 or more points, indicating a very severe impact on the QoL of these women.

Table 4: Impact of urinary incontinence on quality of life and severity of urinary loss related to daily activities (ICIQ-SF).

Variable	n=32
QoL impact, n (%)	
Mild (1-3 points)	3 (9.4)
Moderate (4 - 6 points)	9 (28.1)
Severe (7-9 points)	7 (21.9)
Very severe (10 or more points)	13 (40.6)
When does urine leak? n (%)	
Leaks before you can get to the toilet	10 (31.3)
Leaks when you cough or sneeze	32 (100)
Leaks when you are asleep	2 (6.3)
Leaks when you are physically active/ exercising	3 (9.4)

UI=Urinary Incontinence, QoL=Quality of Life, CF=Cystic Fibrosis, n=number of cases

Also, in logistic regression analysis for UI, there was no significant association for age, BMI, FEV 1, FVC, sputum bacteriology and LCQ total score.

Discussion

In the present study, 52 adult women with CF were evaluated to verify the prevalence of UI and its associations with QoL, cough score, nutritional aspects and pulmonary function. UI was present in 61.5% of the women with CF, 44.2% with SUI and 17.3% of the mixed UI. The presence of UI was significantly associated with low QoL. However, there was no association between UI and pulmonary function, sputum bacteriology, and cough score.

UI has been shown to be prevalent in adult women with CF, a systematic review of 2017 reports that most published research focuses on adult women with CF, where the reported prevalence of UI ranges from 30% to 76% [4] in this study we found a prevalence of 61.5% of UI in women with CF.

SUI is recognized as a common complication in women with CF, presenting a prevalence of 30% to 69% [6]. In the present study, the prevalence of SUI was 44.2%. In CF, due to the high prevalence of cough and increased intra-abdominal pressure, which progressively overloads the pelvic floor musculature, can cause SUI with a negative impact on patients' QoL [16]. In this study, the prevalence of MUI was found in 17% of the women, corroborating previous studies [7,15].

[17] In a recent study evaluated the urinary incontinence in women with clinically stable chronic lung disease comparing with healthy women. The authors demonstrated that most of women in all three groups reported episodes of incontinence (CF 71%; chronic obstructive pulmonary disease 70%; healthy women 55%). Women with CF reported more episodes of incontinence and stress incontinence compared to age-matched healthy controls. The presence of chronic lung disease was considered an independent predictor of incontinence in women.

Interestingly, our study did not find any association between severities of lung disease as measured by FEV 1% predicted, sputum bacteriology and BMI and symptoms of UI. In accordance with our findings, the study of [17] found no association between UI with BMI and FEV 1. The mechanisms of incontinence in CF are likely to be multifactorial. Pelvic floor muscles do not work in isolation for the maintenance of continence but act synergistically with all muscles of the abdomino-pelvic cavity to contribute to spinal stability, intra-abdominal pressure and continence [18]. Genetic causes, age, female gender, chronic cough and constipation are potential factors which may influence the failure of this mechanism to preserve continence in CF subjects [7].

It is important to evaluate the impact and perception of QoL in women with UI. Several studies have concluded that women with UI frequently present a decrease in their QoL [4,8]. In this study, a significant association between UI and QoL was found by KHQ (domains health perception, personal life, task limitation, physical limitations, social limitations, personal relationships, emotions, and sleep and severity measures). In ICIQ-SF, 41% of incontinent women scored 10 or more points, showing that UI had a very serious impact on the QoL of women with UI, As shown in this study, 41% of the women reported that the daily frequency increase "greatly affects" their life; in nocturia 25% reported that it "affects a little"; in the urge 12.5% reported that "it affects a lot", in the overactive bladder most reported that "affects more or less", in stress UI 62.5% reported that "affects a little", corroborating with other findings [9,15]. In this study the main cause of urinary loss reported in ICIQ-SF was coughing and sneezing, all women classified as incontinent lose urine in this situation, which correlates with studies [15] where 84% lost urine through cough and sneezing. No significant association was found between UI and QoL assessed by LCQ. The results of the LCQ may have been limited because they are adult women with CF adapted to the symptoms of chronic cough and in the phase of disease stability.

This study has several limitations. First it was conducted in a single center with small sample size. Secondly, the cross-sectional design prevents the examination of temporal relationships between UI and QoL. In conclusion, this study identified a high prevalence of UI in women with CF. The presence of UI resulted in a negative impact on QoL in women with CF. Health professionals should be prepared to see the patient as a whole, with more attention to extrapulmonary issues. The high prevalence and negative impacts of incontinence in women with CF draw attention to the need for screening of pelvic floor dysfunction and referral for treatment at a specialist service.

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