Non-Pulmonary Chronic Diseases in Adults with Cystic Fibrosis: Analysis of Data from the Cystic Fibrosis Registry

Abstract

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The international literature shows that the demography of cystic fibrosis (CF) is changing, with patients increasingly surviving into adulthood. As they age, patients with CF become more susceptible to specific non-pulmonary chronic diseases. In this study, adult data from the CF Registry of Ireland (CFRI) was used to determine the prevalence and associated features of these diseases. 104 (25.7%) adults had diabetes versus 13 (2.9%) children (p<0.001). Liver disease was present in 47 (11.6%) adults and 26 (5.7%) children (p=0.002). 173 (42.7%) adults had bone disease versus 25 (5.5%) children (p<0.001). Adults with one non-pulmonary chronic disease, for example liver disease, were more likely to have another (p=0.002), those with diabetes and bone disease had a higher number of hospital admissions in the last 12 months (p=0.001 for both) and higher rates of depression (p=0.046 and p=0.049, respectively). These results highlight a number of challenges for the Irish healthcare system.

Introduction

Ireland has the highest rate of CF in the world, with an estimated incidence of 1/1353 and prevalence of 2.98/10,000.1-2 Although CF is still the most frequently diagnosed fatal genetic illness in Caucasians, life expectancy has improved dramatically in recent decades. The median survival for Irish males and females born in 1985-1994 is now predicted to be 1 and 39.6 years, respectively.3,4 This increased longevity has translated into an increase in the Irish adult CF population from approximately 2% per year since 2002.5-7 The three main non-pulmonary chronic diseases associated with CF are diabetes, liver disease and bone disease. The incidence of diabetes and bone disease increases with age, whereas liver disease is usually diagnosed in childhood. The prevalence of diabetes is reported to be approximately 36% in adults aged 18-30 and 52% in adults aged >40.8-10 Approximately 20-60% of CF patients have some evidence of liver disease and 5-15% develop cirrhosis.11-13 Among patients aged >23.5% of adults with CF are estimated to have osteoporosis and 36% osteopenia.14 As patients grow older, it can be expected that these non-pulmonary CF related chronic diseases will become a greater source of morbidity among this adult population.

Methods

This study used data from the CFRI, including all patients alive on 31/12/2009. The aims were: to describe the demographics of the Irish adult CF population, to assess the prevalence of diabetes, liver disease and osteoporosis/osteopenia in adult patients and to compare these with the paediatric population and to identify the demographic and clinical features of these diseases in the adult population.

Since 2001, the CFRI has gathered clinical and demographic information on all enrolled people with CF in Ireland, both demographic and clinical features of these diseases in the adult population.

Results

Demographics of the Adult CF Population

Of the 1027 patients with CF who were enrolled with the CFRI and alive on 31/12/2009; 531 (51.7%) were e18 years of age (range 18-59). 312 (58.8%) were male and there was no significant difference in the distribution of the sexes across the age groups (p=0.284). Of the 1027 patients enrolled in 2010, 90% of the Irish CF population were enrolled in the analysis. The variables included in this analysis were: age, gender, CF genotype, highest forced expiratory volume in one second (FEV1) of 2009, highest body mass index (BMI) of 2009, number of hospitalisations and respiratory exacerbations requiring intravenous (IV) antibiotics in the last one year. CF RI staff, in the absence of specific information, classified diabetes (hereafter referred to as respiratory exacerbations) is recorded as the number of times IV antibiotics were prescribed for a respiratory exacerbation and diabetes is recorded as present if the patient is documented as being on insulin in the last year, whereas liver disease, depression and osteoporosis/osteopenia (recorded together) are considered present if documented in the medical notes in the last year. Chronic infection is considered present if the patient has had 3 or more documented isolates of the organism in the last year. In the case of Pseudomonas, this includes all types of Pseudomonas organisms.

Adults were defined as those e18 years of age; those <18 were considered children. Age was used as a continuous variable in regression analysis, and in other adult analyses age was examined in two ways. To give an overall view of 5 year age groups were created with the e40 year old patients grouped together due to small numbers. Given that patients over 40 may differ systematically from younger patients, a variable with two groups was also created, greater than/equal to or less than 40 years old. Proportions in groups were compared using student’s t test for two groups and ANOVA for more than two groups. Where values were not normally distributed, the Mann-Whitney U test was used to compare medians in groups. Adjusted means were obtained using ANCOVA. Logistic regression was used to adjust for confounders and variables which had a significance of p<0.10 on univariate analysis were entered into the multivariable models. A p value of <0.05 was taken to be significant.

Diabetes

In the adult population, there was no significant difference in the prevalence of diabetes between the sexes (p=0.258) or the age groups (p=0.006). Diabetic patients had a higher median number of admissions (p=0.001) and respiratory exacerbations (p=0.023) and a higher prevalence of chronic Pseudomonas infection (72.1% versus 58.8%, p=0.016). Values of diabetic patients were lower, but did not reach statistical significance.7,10 (6.7%) adults with diabetes had depression, versus 6/301 (2.0%) of those without (p=0.044). The results of the univariate logistic regression analysis for factors associated with diabetes in adults are shown in Table 1. All variables with a statistical significance of p<0.1 on univariate analysis except pancreatic insufficiency; 7,10 7%580 homozygous, bone disease and liver disease were significant in the final model (Table 2, model one). When pancreatic insufficiency was added to this model all other relationships became insignificant (Table 2, model two) indicating that the relationships are confounded by the strong inter-relationships between diabetes, pancreatic insufficiency and 7%580 homozygosity.

Liver Disease

Among the adult patients, there was a significant association between liver disease and 7%580 homozygosity (p=0.018) but not sex (p=0.128). There were significant associations between liver disease and diabetes and osteoporosis/osteopenia (p=0.002 for both, Figure 2).

Osteoporosis/Osteopenia

In the adult population, there was no significant association between osteoporosis/osteopenia and 7%580 homozygosity (p=0.191) or sex (p=0.411) but those with bone disease had a higher prevalence of chronic Pseudomonas infection (68.8%...
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Discussion

Over half (51.7%) of the patients in this study were e18 years of age. This is in keeping with the documented increase in the adult CF population both in Ireland, with 49% aged 18 years in 2007 and 52.7% in 2010, such as in the CF Registry. The need to review services in Ireland in order to ensure they are meeting the needs of the adult CF population has been recognised by many organisations, including the CFRI.20 A 2009 Health Service Executive report commented that inequalities across CF services and the need to prioritise improvement of adult services, as well as this, the concept of transition of care from paediatric services is clearly important.

Bone disease reported in this study is in keeping with the literature. The prevalence of diabetes and liver disease are likely to be underestimated in those with subclinical disease, due to the way in which data are collected. While the burden of non-pulmonary chronic disease on individuals with CF cannot be assessed from a study such as this, the analysis shows some interesting findings. A relationship between diabetes and liver disease in CF has previously been shown both in Europe and the United States and this study confirms that patients with one non-pulmonary chronic disease are more likely to be diagnosed with another. Those with diabetes or bone disease were also more likely to have been admitted to hospital in the last 12 months. This increased number of hospitalisations may be due to ascertainment bias, as patients who are hospitalised more frequently are more likely to have comorbidities picked up. It may also reflect increased severity of disease. The risk of death in CF adults, especially in those with lower lung function has been previously documented. Although small numbers prohibited more detailed analysis, this study suggests a link between non-pulmonary CF-related chronic diseases and depression. Further research is needed, as depression may be underreported from studies such as this which rely on documented diagnoses as opposed to scores from validated instruments.

In summary, while great advances have been made in CF care, which have translated into increased longevity, it is important to consider the challenges this has brought. Improving survival does not just to individual patients, but also to the Irish healthcare system and health care professionals in all areas of adult medicine, who may become more likely to encounter CF patients in their daily practice.

This study highlights the need to continue to invest in adult CF care, in what have historically been underfunded services. As well as research into the causes and prevention, screening and management strategies for these non-pulmonary chronic diseases could provide new avenues in CF care and help ensure that increasing quality of life is matched by a good quality of life for patients with CF.

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References