Comorbidity, disease burden and mortality across age groups in a Swedish primary care asthma population: An epidemiological register study (PACEHR)

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ABSTRACT

Background: Asthma is often associated with other diseases. To identify and manage comorbidities is important, as these conditions may increase the disease burden.

Objective: To describe the prevalence of comorbidities, disease burden and mortality across age groups in a large Swedish primary care real-life asthma population.

Methods: Observational cohort study of asthma patients, all ages, identified from electronic medical records by ICD-10-CM code, data from 36 primary care centers. Data were linked to national mandatory Swedish health registers. Comorbidities were identified by ICD-10-CM codes and collected from electronic medical records and the National Patient Registers, mortality data from the Cause of Death Register. Exacerbations were defined as hospitalizations due to asthma, and/or emergency visits at hospital and/or prescription claims of oral steroids.

Results: In total 33,468 patients (58% women) were included. The most prevalent comorbidities were acute upper respiratory tract infection (53%), rhinitis (25%), acute lower respiratory tract infection (25%), hypertension (21%), anxiety and depression (20%). The comorbidities associated with highest risk for an exacerbation were COPD OR 1.98 (95%CI: 1.80–2.19), nasal polyps OR 1.75 (95%CI: 1.49–2.05) and rhinitis OR 1.52 (95%CI: 1.41–1.63). All-cause mortality was similar to the Swedish population, 1011 deaths per 100,000 person/year compared with 1058 deaths (standardized risk = 0.99 [95%CI:0.95–1.04]). The pulmonary related death rate was greater in the study population versus the Swedish population (122 versus 72 per 100,000 person/year).

Conclusion: Comorbid disease was frequent in this large real-life asthma population with an impact on exacerbations. To identify and treat comorbidities with impact on asthma outcomes are essential to improve asthma care.

1. Introduction

Asthma is a common disease, often associated with other conditions occurring concomitantly. In asthma care, it is important to identify and manage comorbidities, as these conditions may increase symptoms, impair quality of life and increase the risk of medical interactions [1].

Comorbidity is often defined in relation to an index disease or condition [2] whereas multimorbidity is referred to as the co-occurrence of multiple chronic or acute diseases and medical conditions in one person without reference to an index condition [3]. These two entities reflect different ways of approaching management of patients with more than one disease, where the former may be more relevant in secondary care and the latter in primary care [4]. Most health care systems, especially in secondary care, are structured for individual diseases rather than multimorbidity [5]. In this study, we will use the term comorbidity.

Prevalence of comorbidity was studied using medical practices data from primary care in a large study from Scottish medical practices showing that 42% of all patients had one or more morbidities and 23% were multimorbid which increased with age [5]. Of those with

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multimorbidity more than half were younger than 65 years and there was a strong association with low socio-economic status [5].

Detecting and defining comorbidities and their impact on patients with asthma is important when assessing the disease burden [4]. In a population based Canadian study individuals with asthma had a greater frequency of comorbidities than individuals without asthma and a high utilization of health care [6]. Asthma comorbidity has in several studies been associated with poor asthma control, unscheduled care and impaired health related quality of life [6–8]. Outcome of asthma management is also dependent on treatment of comorbidities [9]. In individuals with severe asthma, comorbidities are common, and can lead to worsening of asthma symptoms and control [10].

Asthma mortality has decreased during the last twenty years, probably owing to improved management and treatment, particularly due to the beneficial effects of inhaled corticosteroids [11]. Despite this, results from a Canadian study show that individuals with asthma had greater all-cause mortality compared with the general population [12].

Considering the impact of comorbidities on a life-long asthma disease, knowledge of which diseases that are most common in different ages and have most influence on asthma outcomes would be of great interest. The aim of this study was to describe the prevalence of comorbidities, disease burden and mortality across age groups in a large Swedish primary care real-life asthma population.

2. Methods

In Sweden, the healthcare organisation is primary care based, and the majority of adult patients with asthma are diagnosed and managed in primary care, with referrals to secondary care only in cases of severe and difficult to treat asthma [13]. In this observational cohort study asthma patients were identified from primary care medical records data from 36 primary care centers (PCC). These data were linked to data from national mandatory Swedish health registers (the National Patient Register, the Cause of Death Register, and the Swedish Prescribed Drug Register). Included centers cover a mix of rural and urban areas, public and private providers, and center size. Electronic medical records data, e.g. date of birth, sex, primary health care contacts, spirometry measurements, and diagnoses of asthma and comorbidities by ICD-10-CM codes and drug prescriptions, extracted using an established software system (Pygargus Customized eXtraction0, Program, CXP®) [14], were linked to data from Swedish national health registers, covering mandatory individual health data. Data regarding morbidity were also collected from the National Patient Register, inpatient hospital care and outpatient hospital care (admission and discharge dates, main and secondary diagnoses specified by ICD-10-CM code), and mortality from the Cause of Death Register (date and cause[s] of death), respectively. Data on medication claims were collected from the Swedish Prescribed Drug Register. The personal identification number used to identify included patients was replaced with a study ID number prior to further data processing. Data linkage was performed by the Swedish National Board of Health and Welfare. The linked database was managed by the Department of Medical Sciences, Respiratory Medicine at Uppsala University, Sweden. The study protocol was reviewed and approved by the regional ethics committee in Uppsala, Sweden (reference number 2014/446).

2.1. Study population

All male and female patients above the age of six years with a physician-diagnosed asthma (ICD-10 code J45–J46) at any time prior to 2014, were included. Patients below the age of 6 years with a diagnosis of asthma were also included if they had an asthma diagnosis recorded after the age of 6 years.

There were no other exclusion criteria. Patients were followed from 1st of January 2006 to 31st of December 2013 or until emigration or death, and were stratified into seven clinically relevant age groups; < 7, 7–14, 15–29, 30–49, 50–64, 65–74, and ≥75 years.

2.2. Outcomes and variables

Comorbidities (cumulative prevalence), based on physician diagnosis, were identified using ICD-10 codes (Acute upper respiratory tract infections (J00–J06), Rhinitis (J30–J32), Nasal polyps (J33), Acute lower respiratory infections (J20–J22), COPD (J43–J44), Pneumonia (J11–J18), Diabetes type 2 (E11), Metabolic disorders (E70–E90), Hypertensive diseases (I10–I15), Ischaemic heart disease (I20–I25), Heart failure (I50), Rheumatoid arthritis (M05–M06), Polymyalgia rheumatica (M35.3), Anxiety and Depression (F41, F32), Osteoporosis (M80–M82), Inflammatory bowel disease (K50–K52).

Medications were defined by ATC codes (inhaled corticosteroids (ICS) (R03BA), short-acting β2-agonists (SABA) (R3AC02–03), long-acting β2-agonists (LABA) (R03AC12-13,17–18, R03CC12), long-acting muscarinic antagonist (LAMA) (R03BB04, fixed ICS/LABA combination (R03AK), leukotriene receptor antagonists (LTRA) (R03DC), oral corticosteroids (H02AB), cardiovascular medications (C), statins (C10AA, beta-blockers (C07), angiotensin-converting enzyme inhibitor (C09A-B), angiotensin II receptor antagonist (C09C-D), respiratory antibiotics (J01AA, J01CA), antihistamines (R06), nasal corticosteroids (R01AD), antidepressants (N06A), anxiolytics (N05C)).

Lung function data were assessed from the electronic medical records, and if more than one lung function measurement, expressed as post-bronchodilator FEV1% predicted value, was available within a year, the highest value was used.

Exacerbations were defined as hospitalizations because of asthma, and/or emergency visits at hospital and/or prescription claims of oral steroids in primary or secondary care. Repeated exacerbations occurring within 14 days were calculated as one single event.

Mortality and cause of death were identified according to the Cause of Death register for years 2006–2013.

2.3. Statistical analyses

Statistical analyses were performed using SAS version 9.3 and R version 3.2.3. Patient characteristics for the 2013 asthma population are described as mean (SD) for continuous variables and absolute and relative frequencies for categorical variables.

The risk of having an exacerbation during the year 2013 was analyzed using a logistic regression model with specific comorbidities prior to 2013 as independent variables. The analyses have been performed in two steps. First all comorbidities were analyzed in a univariate model and then all variables with a p-value < 0.05 were entered into a multivariable model.

Standardized death was calculated using an indirect standardization method using the distribution of the Swedish population in 2013 as a reference.

3. Results

Overall, 33,468 asthma patients with a mean age at asthma diagnosis of 42.4 years (58% women) were included. Mean FEV1 was 84.6% of predicted value and exacerbation rate was on average 27.2 exacerbation events per 100-patient-years (Table 1).

The exacerbations increased with age from 13.4 (events/year/100 patients) among those 15–29 years old to 51.3 in those above the age of 75. The most prevalent comorbidities were acute upper respiratory tract infection (53%), rhinitis (25%), acute lower respiratory tract infection (25%), hypertension (21%), anxiety and depression (20%), pneumonia (16%), metabolic disorders (12%), COPD (8%), diabetes type 2 (6%), ischemic heart disease (6%), and heart failure (4%) (Fig. 1).

The number of co-morbidities increased with age. The majority of the patients in age groups up to 64 years had two comorbidities or less,
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