

Prevalence and incidence of keratoconus in Sweden: A nationwide register study between 2010 and 2020

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Abstract

The purpose of this study was to estimate the prevalence and incidence of keratoconus in Sweden. The study had a cross-sectional descriptive design, using data from the Swedish Patient Register. Data about keratoconus registered from 1st January, 2010, to 31st December, 2020, were analysed. Prevalence was estimated from the total number of patients registered. Incidence was estimated from the number of first-time registrations per year for the age group 0 to 40 years and stratified by decades of age.

From 2010 to 2020, 16,055 patients were registered with keratoconus in the Swedish Patient Register, giving a total estimated keratoconus prevalence of 169.5 per 100,000 (95% CI: 144.9–194.1), 74.2% were male. The estimated annual incidence of keratoconus was 11.8 per 100,000 (95% CI: 5.1–18.5). The average annual incidence was highest in the decade 21 to 30 years, 26.1 per 100,000 (95% CI: 16.1–36.1). For the age group 0 to 40 years, the estimated incidence of keratoconus was 22.5 per 100,000 (95% CI: 13.7–32.3).

Keratoconus should not be regarded as an uncommon condition. The prevalence of keratoconus may be even higher because of under-registration among older citizens. The estimated prevalence and incidence of keratoconus in Sweden is comparable to estimated prevalence in Norway.

Keywords: Keratoconus, prevalence, incidence, epidemiology

Introduction

Keratoconus was first described in 1854 as a non-inflammatory and chronic corneal ectasia (Gordon-Shaag et al., 2015). It is characterised by progressive steepening and thinning of the cornea that can lead to visual impairment (Mukhtar & Ambati, 2018). Two decades ago, corneal collagen crosslinking (CXL) was introduced, revolutionising the treatment to prevent the progression of keratoconus (Gregor et al., 2003; Kankariya et al., 2013).

Keratoconus often presents unilaterally and patients are often asymptomatic in the early stages of keratoconus. However, within 16 years more than half of the unaffected eyes develop keratoconus (Kankariya et al., 2013; Mukhtar & Ambati, 2018). During the progression of keratoconus, myopia and irregular astigmatism develop causing decreased visual acuity, therefore keratoconus is often first detected in the course of an eye examination (Gordon-Shaag et al., 2015).

The number of detected new cases of keratoconus has increased in the last decade because of more advanced diagnostic tools available to monitor corneal ectasia (Flynn et al., 2016). The best and most sensitive method for the detection, diagnosis and follow-up of keratoconus is corneal topography (Gordon-Shaag et al., 2015). Previous studies estimate the prevalence of keratoconus to be 50 to 54 per 100,000 worldwide (Kennedy et

al., 1986; Romero-Jiménez et al., 2010). However, a recent study from the Netherlands estimated a keratoconus prevalence of 265 per 100,000 (Godefrooij et al., 2017). In Scandinavia, the reported prevalence of keratoconus in Norway is 192.1 per 100,000 and in Denmark 44 per 100,000 (Bak-Nielsen et al., 2019a; Kristianslund et al., 2020). The annual overall incidence of keratoconus in Norway was found to be 19.8 per 100,000 and the highest rate of new cases, 36.7 per 100,000, was in the age group from 21 to 30 years (Kristianslund et al., 2020). In Denmark, the annual incidence of keratoconus was estimated to be 3.6 per 100,000 (Bak-Nielsen et al., 2019b). To our knowledge, no studies report the prevalence and incidence of keratoconus in Sweden. The aim of this paper is to present an estimated prevalence and incidence of keratoconus in Sweden between 2010 to 2020.

Methods

The study had a cross-sectional, descriptive design, analysing data obtained from the Swedish Patient Register administered by the Swedish National Board of Health and Welfare. Since the establishment of the International Classification of Disease and Related Health Problems (ICD-10) in 2011, it has been mandatory for Swedish healthcare practitioners to report diagnoses and treatment to the Patient Register. Further, in the same period, CXL has been introduced as a treatment for keratoconus.

The study population was all men and women with keratoconus in Sweden. The sample population was men and women registered with a diagnosis of keratoconus in the Swedish Patient Register between 2010 to 2020. Each patient has a unique patient identifier in the register. Information on age and gender was collected.

The present study analysed data for all patients registered with the ICD-10 code for keratoconus H18.6. Data were obtained for the period from 1st January 2010 to 31st December 2020. Further, the study used data on gender and age for the population of Sweden obtained from the open digital archive at the Central Bureau of Statistics (www.scb.se) for the analysis.

The prevalence of keratoconus was estimated based on the total number of patients registered with keratoconus between 2010 and 2020 (inclusively) and the average number of inhabitants in Sweden in the same period. The incidence was based on the number of new registrations of keratoconus each year and the number of inhabitants in Sweden each year. Further, the incidence was estimated for the age group 0 to 40 years, according to the likely age at onset of keratoconus and to allow for comparison with previous studies (Godefrooij et al., 2017; Kristianslund et al., 2020), and incidence was stratified for age groups 0–20, 21–30, 31–40, 41–50, 51–60, 61–70, 71+ years.

Data were analysed using the free software program R-commander (version 2.8.1) and estimates were presented per 100,000 inhabitants, with a 95% confidence interval (CI).

The study adhered to the Declaration of Helsinki. The Swedish Ethical Review waived the need for study approval. The Swedish National Board of Health and Welfare approved the use of anonymous data.

Results

From 2010 to 2020, 16,055 patients were registered with ICD-10-code H18.6 Keratoconus in the Swedish Patient Register, 74.2% were male. During the same time period, the average number of inhabitants of Sweden was 9,886,365. The estimated overall prevalence of keratoconus was 169.5 per 100,000 (95% CI: 144.9–

194.1). Table 1 presents the total and age-stratified prevalence of keratoconus. The prevalence was highest in the age group 21 to 30 years, 348.4 per 100,000 (95% CI: 313.2–383.6), and lowest among patients older than 70 years, 63.8 per 100,000 (95% CI: 48.8–78.8).

Table 1: The estimated average and age-stratified prevalence of keratoconus.

Age groups (years)	Prevalence per 100 000 (95% CI: lower to upper)
0–20	90.0 (71.8–108.2)
21–30	348.4 (313.2–383.6)
31–40	255.3 (225.2–285.4)
41–50	183.8 (158.3–209.3)
51–60	133.5 (111.8–155.2)
61–70	111.5 (91.7–131.3)
71+	63.8 (48.8–78.8)
All	169.5 (144.9–194.1)

Figure 1 shows the number of first-time registrations for each year. The estimated average annual incidence of keratoconus was 11.8 per 100,000 (95% CI: 5.1–18.5), ranging from 5.2 per 100,000 (95% CI: 0.8–9.7) in patients older than 70 years to 26.1 per 100,000 (95% CI: 16.1–36.1) in patients aged 21 to 30 years (see Figure 2). From 2010 to 2020, the average estimated incidence of keratoconus in the age group 0 to 40 years was 22.5 per 100,000 (95% CI: 13.7–32.3), with the annual incidence varying from 18.5% to 25.4% (see Figure 3).

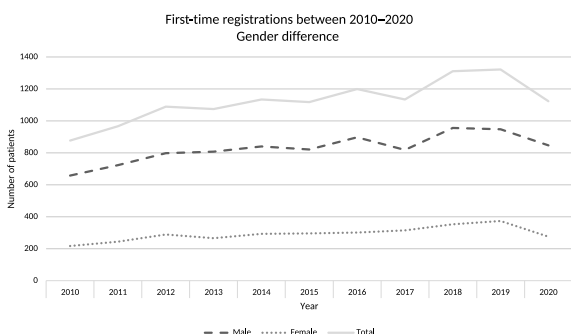


Figure 1: Total number of first-time registrations by year from 2010 to 2020.

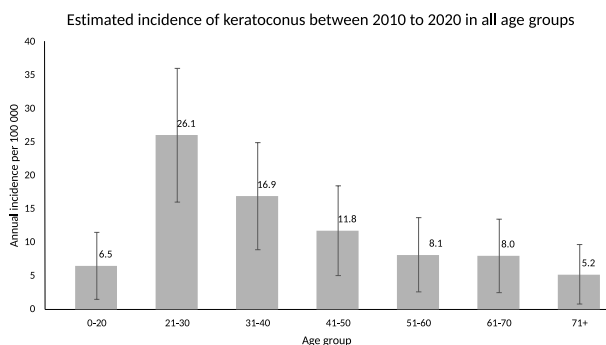


Figure 2: The age-stratified average annual incidence of keratoconus from 2010 to 2020.

Discussion

To our knowledge, the prevalence and incidence of keratoconus in Sweden have not previously been reported. The estimated prevalence of keratoconus in Sweden of 169.5 per 100,000 is three times higher than earlier reported estimates of 54 per 100,000 (Kennedy et al., 1986; Romero-Jiménez et al., 2010). Our findings reflect an increased prevalence of keratoconus similar to the estimated prevalence in Norway and the Netherlands,

192.1 per 100,000 and 265 per 100,000 respectively (Godefrooij et al., 2017; Kristianslund et al., 2020). In Denmark, the estimated prevalence of keratoconus for the period 1975 to 2015 was 44 per 100,000, reflecting previous estimates (Bak-Nielsen et al., 2019a). The increased prevalence in our study, and the Dutch and Norwegian studies, may be related to greater numbers of case findings of keratoconus in optometric practice, better access to eye care, better defined diagnostic criteria for keratoconus, improved diagnostic methods, increased availability of CXL treatment, as well as changes in the ethnical origin of the population. As Sweden, Norway and Denmark are countries with similar healthcare systems and populations, the discrepancies in prevalence of keratoconus may be due to differences in optometric practice, diagnostic criteria, and diagnostic methods in ophthalmic healthcare.

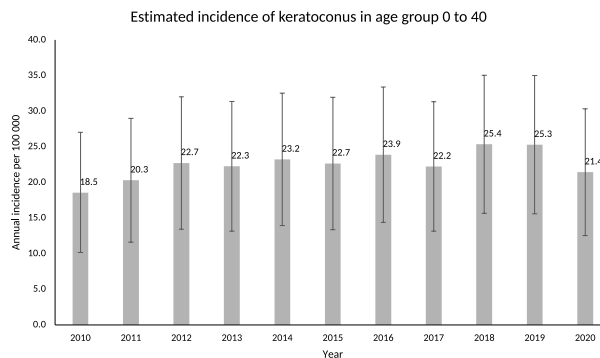


Figure 3: Estimated annual incidence of keratoconus for the age group 0 to 40 years.

Three out of four patients registered with keratoconus in Sweden were male, which is in line with current findings from Norway, Denmark, the Netherlands, and other studies showing a clear overrepresentation of keratoconus among male patients (Aylin & Orkun, 2008; Bak-Nielsen et al., 2019b; Godefrooij et al., 2017; Kristianslund et al., 2020). There are no clear explanations for the possible gender difference in keratoconus, although there is a hypothesis that hormonal factors may be an explanation (Gordon-Shaag et al., 2015). However, some studies have found no or only a small gender difference for prevalence of keratoconus (Hwang et al., 2018; Kennedy et al., 1986; Xu et al., 2012). For some of these studies, this may be due to a different ethnical background of the study population (Hwang et al., 2018; Xu et al., 2012).

The present study estimates an average keratoconus incidence of 11.8 per 100,000, with the highest incidence in the age group 21 to 30 years (26.1 per 100,000) and the second highest incidence in the age group 31 to 40 years (16.9 per 100,000). These results are supported by the study from Norway that presents similar distribution in the same age groups (Kristianslund et al., 2020). The lower incidence in the older age groups likely reflects that these patients were diagnosed before the implementation of the register. In the age group 0 to 20 years, the incidence was low compared to age groups 21 to 30 years and 31 to 40 years, and it is known that keratoconus debuts around puberty to young adulthood. The lower incidence in the youngest age group may reflect the fact that keratoconus takes some years to progress before it has an impact on vision. Moreover, suspected cases found in patients aged 20 to 40 years by optometrists may be related to visual requirements for driving or work. Nevertheless, it is important to screen for keratoconus in young patients as keratoconus can lead to reduced visual acuity, negatively affecting educational and social development (Mukhtar & Ambati, 2018).

It is assumed that the patients in our study with first-time registration of keratoconus in late adulthood have been undiagnosed in the greater part of their life, so to adjust for these as-

pects, a secondary estimation of incidence for patients aged 0 to 40 years was made. The estimated incidence in the age group 0 to 40 was 22.5 per 100 000, which is higher than the average incidence, and likely represents a more accurate incidence of keratoconus. This incidence is comparable to the estimated incidence in Norway and Netherlands, 19.8 per 100 000 aged 0 to 40 years and 13.3 per 100 000 aged 10 to 40, respectively (Godefrooij et al., 2017; Kristianslund et al., 2020).

In the present study, the number of first-time registrations of keratoconus has increased from 2010 to 2020, which is in line with reports from Norway (Kristianslund et al., 2020). This increase in incidence likely reflects greater awareness and improved diagnostic tests for keratoconus. Further, research about keratoconus has resulted in modern grading systems like Belin being implemented in diagnostic instrument software, which has made it easier to detect and follow progression in patients with keratoconus (Belin et al., 2020). This enhanced system of grading has also been implemented in diagnostic instrument software (Pentacam, Oculus GmbH, Wetzlar, Germany) to facilitate the grading of keratoconus (Belin et al., 2020).

In 2020, there was a slightly reduced incidence of keratoconus in Sweden, and we propose this was due to the Covid-19 pandemic leading to delayed diagnosis of keratoconus. Delayed diagnosis and management of keratoconus can lead to preventable reduction in visual acuity, and thereby reduction in quality of life. Therefore, it is important for clinicians, and policymakers allocating healthcare personnel, to prioritise appropriately, both during a pandemic and under normal circumstances. This is also highlighted as an important topic in a Norwegian population study (Kristianslund et al., 2020).

The study has some limitations. First, it does not explore ethnicity or immigration, which have been described as factors impacting the prevalence of keratoconus. In the Norwegian study, Kristianslund et al. (2020) suggested that the increased prevalence of keratoconus could be a result of immigration from regions with a higher prevalence of keratoconus, like Africa and Asia. The Danish study found a lower incidence of keratoconus when immigrants were excluded from the data analysis (Bak-Nielsen et al., 2019b). Further, the Dutch study presents a high prevalence and reports that approximately 22% of the general population was immigrants. Therefore, it is suggested that further epidemiological studies where information about ethnicity is included, should be carried out to improve the knowledge about keratoconus in Sweden. Second, the data were obtained by ICD-10 codes, specifically H18.6 keratoconus. There are other corneal ectasias with separate ICD-10 codes. Nevertheless, some of these cases may have been coded as keratoconus cases and included in our data. The number of these is low compared to the number of keratoconus cases, and therefore has a limited impact on the findings of the present study. Third, the diagnostic methods and diagnostic criteria (grading system) may influence the first-time diagnosis of keratoconus. To our knowledge, there are no general guidelines for diagnosis and management of keratoconus in Swedish healthcare. However, we believe the lack of general guidelines had limited impact on the data in the present study. Fourth, the study did not obtain first-time diagnostic outcome measurements such as pachymetry, keratometry or visual acuity that could have determined the stage of keratoconus at the time of diagnosis. A more in-depth study including this data could indicate if keratoconus was diagnosed at an early stage or if there is a need for improvement in detection and early management of keratoconus. Fifth, ICD-10 codes can be used by general practitioners or other health personnel suspecting keratoconus and referring patients to an ophthalmologist. The ophthalmologist may later contradict the diagnosis. This first ICD-10 code will be recorded in the Patient Register and contribute to an overestimation of

keratoconus in the population. However, we believe this will have had limited impact on the data in the present study.

The results of the present study suggest an increase in keratoconus cases in Sweden between 2010 and 2020. The prevalence and incidence of keratoconus in Sweden are higher than reported in some review studies, but comparable to a recent Norwegian study. The true prevalence may be even higher due to under-registration in older age groups. The results of the present study indicate that keratoconus should not be regarded as an uncommon condition in Sweden.

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Prevalens og forekomst av keratokonus i Sverige: En nasjonal registerstudie for perioden 2010–2020

Sammendrag

Hensikten med denne studien var å estimere forekomst og antall nye tilfeller av keratokonus i Sverige. Studien hadde et deskriptivt tverrsnittdesign, og benyttet data fra det svenske pasientregisteret. Data om keratokonus registrert i perioden fra 1. januar 2010 til 31. desember 2020 ble analysert. Forekomst ble estimert fra det totale antallet registrerte pasienter. Insidens, antall nye tilfeller, ble estimert ut fra antall førstegangsregistreringer per år, tiårsklasse og for aldersgruppen 0 til 40 år.

Fra 2010 til 2020 ble 16 055 pasienter registrert med keratokonus i det svenske pasientregisteret, noe som ga en estimert total forekomst av keratokonus på 169,5 per 100 000 (95% KI: 144,9–194,1), 74,2% var menn. Estimert antall nye tilfeller av keratokonus per år var 11,8 per 100 000 (95% KI: 5,1–18,5). Gjennomsnittlig antall nye tilfeller var høyest i aldersgruppen 21 til 30 år, 26,1 per 100 000 (95% KI: 16,1–36,1). For aldersgruppen 0 til 40 år var estimert antall nye tilfeller per år 22,5 per 100 000 (95% KI: 13,7–32,3).

Keratokonus bør ikke ansees som en sjelden tilstand. Forekomsten av keratokonus kan være enda høyere på grunn av underregistrering blant eldre borgere. Estimert forekomst og antall nye tilfeller av keratokonus i Sverige er sammenliknbare med estimert forekomst og antall nye tilfeller i Norge.

Nøkkelord: Keratokonus, prevalens, insidens, epidemiologi

Prevalenza ed incidenza del cheratocono in Svezia: uno studio e registro nazionale tra il 2010 e il 2020

Riassunto

Lo scopo di questo studio è di determinare la prevalenza ed incidenza del cheratocono in Svezia. Lo studio è di tipo descrittivo considerando un disegno sezionale ed incrociato utilizzando dati del registro dei pazienti svedesi. Dati sul cheratocono registrati tra il primo Gennaio 2010 e il 31 Dicembre 2020 sono stati analizzati. La prevalenza è stata stimata dal numero totale di pazienti registrati. L'incidenza è stata stimata dal numero dei primi pazienti registrati per anno del gruppo di età dai 0 ai 40 anni e stratificati per ogni decade di età'.

Dal 2010 al 2020, 16,055 pazienti sono stati registrati come cheratocono nel registro dei pazienti svedesi, dando una stima totale della prevalenza di cheratocono di 169.5 per 100,000 (95% CI: 144.9–194.1), di cui il 74.2% sono maschi. La stima dell'incidenza annuale di cheratocono è 11.8 per 100,00 (95% CI: 5.1–18.5). La media annuale di incidenza è la più alta tra la decade 21 a 30 anni, 26.1 per 100,000 (95% CI: 16.1–36.1). Per il gruppo di età' 0 a 40 anni, la stima di incidenza del cheratocono è stata del was 22.5 per 100,000 (95% CI: 13.7–32.3).

Il cheratocono non dovrebbe essere considerato una patologia non-comune. La prevalenza di cheratocono potrebbe essere addirittura più alta per via della sotto-registrazione tra i cittadini più anziani. La prevalenza stimata e l'incidenza del cheratocono in Svezia è comparabile alla prevalenza stimata in Norvegia.

Parole chiave: Cheratocono, prevalenza, incidenza, epidemiologia