

Incidence of Infectious Corneal Ulcers, Portsmouth Study, UK

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Abstract

Aim: To identify the incidence of infectious keratitis in a population based in southern England.

Methods: A retrospective review between January 1997 and December 2003 and a prospective study between January and December 2006 were undertaken at the eye casualty department of Queen Alexandra Hospital (QAH), Portsmouth, UK to identify the incidence of infectious keratitis.

Results: QAH is a tertiary teaching hospital that serves Portsmouth and the catchment area of the county of Hampshire with an average population of 489,391 in the 7 year period of the retrospective study and 499,100 in the one year prospective study. Infectious keratitis occurred in 1,786 patients in the retrospective study with an average of 255 patients per year and in 201 patients in the one year prospective study. The annual incidence of infectious keratitis was 52.1 and 40.3 per 100,000 persons in the retrospective and prospective studies respectively. The rate of bacterial and viral ulcers was lower in the prospective study than the average of either ulcer type in the retrospective study. A significant trend over time was found in the retrospective study that was mainly made by bacterial rather than viral ulcers. The rate of viral ulcers showed initial steady increase between 1997 and 2000 followed by continuous decline over the next three years of the retrospective study and maintained in the prospective study.

Conclusions: Despite widely accepted views of the predominance of viral keratitis in the developed countries, these are decreasing in the population studied and contact lens-related bacterial corneal ulcers are more frequent than viral ulcers.

Keywords: Epidemiology; Contact lens; Cornea; Microbiology; Infection

Introduction

Corneal ulceration is a vision-threatening disease that varies in incidence worldwide. Variation in incidence of infectious keratitis is a multi-factorial issue that includes a tight mix of different factors, such as geographical and other location-related factors [1], degree of development of the country concerned, the predominant predisposing factors and the type of infection commonly present in this community [2]. However, variations in incidence of infectious keratitis have been reported in different keratitis studies conducted in different countries even though these were similar in the degree of development, geographical location, and the most prevalent type of corneal infection and related predisposing factors [3-7]. Moreover, within the same country, France, variations have been reported in the rate of severe forms of infectious keratitis that necessitated hospital admission [3-5].

It is widely accepted that bacterial and fungal keratitis have far higher incidence in the developing world than that in the developed world [8-10]. Also it is thought that viral keratitis is more prevalent in developed countries, such as the United States where Herpes Simplex Keratitis (HSK) is considered the leading cause of corneal blindness [11,12]. However, predominance of bacterial [3,13] and fungal [14-16] keratitis in developed countries has been reported. Moreover, a declining incidence of Herpes Simplex Virus (HSV) eye disease including epithelial and stromal keratitis was recently reported in the USA [17].

Although several studies have investigated different aspects of infectious keratitis, little information is available about incidence of different types of infectious keratitis in large populations. One of the aims of Portsmouth corneal ulceration study was therefore to establish the incidence of different types infectious corneal ulcers in southern England using a large population of patients over several years.

Patients and Methods

A retrospective review between January 1997 and December 2003 and a prospective study between January and December 2006 were undertaken at the eye casualty department of QAH, Portsmouth, UK to identify the incidence of infectious keratitis. The medical records of patients presenting with infectious corneal ulcers to the eye casualty department of QAH in Portsmouth between January 1997 and December 2003 were retrospectively reviewed. In addition, in 2006, a prospective study was undertaken at the same department to confirm the incidence and to detect changes in the frequency of corneal ulceration. The study was conducted according to the declaration of Helsinki and approved from the Isle of Wight, Portsmouth and East Hampshire Local Research Ethics Committee.

A corneal ulcer was defined as a corneal infiltrate associated with an overlying epithelial defect. Corneal scrapes were routinely collected from patients with corneal ulceration in the retrospective and prospective studies for the microbiology assessment unless a clearly diagnostic clinical pattern of ulcer was present.

The corneal scrapes were inoculated onto blood agar, chocolate agar, and fastidious anaerobe agar and brain-heart infusion broth for

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isolation of bacteria; Sabouraud's dextrose agar for isolation of fungi; and nonnutrient *E. coli* enriched agar for isolation of *Acanthamoeba*. Selective media, such as Lowenstein-Jensen for *Nocardia* and Mycobacteria were used if clinically indicated. A positive isolate was defined as a growth along the line of inoculation on solid media or growth in the liquid media that was confirmed by microscopy.

The diagnosis of viral ulcers relied in the majority of cases on the presenting characteristic clinical pattern of viral corneal ulcers. In patients with a suspicious clinical pattern and uncertain diagnosis of viral keratitis, corneal samples were assessed using immunofluorescence.

Incidence values are given per 100,000 per year in the population of Portsmouth area served by the ophthalmology department at QAH. The population of Portsmouth area includes the population of Portsmouth town and the catchment area of the county of Hampshire that includes Fareham, Gosport, Havant, Portchester and Waterlooville. The population of Portsmouth area is given according to the mid-year population estimates given by the Office for National Statistics [18] Chi-square was used for data analyses and p value ≤ 0.05 was considered significant. SPSS software (v11.0) for Windows was used for statistical analysis.

Results

A total of 1,786 patients (3.3%) out of a total 53,341 casualty attendees presented with infectious corneal ulceration between January 1997 and December 2003, with annual and monthly average of patients 255 and 21.3 respectively. The lowest annual number of patients was 208 in 1997 and the highest number was 281 in 2003. A Chi-square goodness of fit test indicates a significant trend over time (Chi-square=14.8, 2df, $p \leq 0.02$) and simple linear regression indicates a significant linear component of trend ($p \leq 0.04$) during the retrospective study.

A total number of 201 patients presented with corneal ulceration during the period of the prospective study between January and December 2006, was lower than the rate of infectious ulcers in any year during the retrospective study. There was 28.5% decline in the total number of patients with infectious corneal ulcers in 2006 compared with the 281 keratitis patients in 2003, the last year of the retrospective study. Also, the total number of patients with infectious corneal ulcers showed a 21.2% decrease in the prospective study than the average 255 patients with corneal ulcers in 7 year-period retrospective study.

The annual incidence of infectious corneal ulcers decreased from 52.1 per 100,000 persons per year in the retrospective study to 40.3 per 100,000 persons in 2006. The average population of Portsmouth area was 489,391 and 499,100 in 7-years period of the retrospective study (1997-2003) and the prospective study in 2006 respectively. In 2006 the incidence of corneal ulcers was lower than the incidence in any year during the retrospective study compared with the upward liner increase in incidence from 42.6 in 1997 to its highest level of 57 in 2003.

Over the period of 7 years of the retrospective study the detected linear trend was mainly related to the bacterial rather than viral ulcers. The rate of bacterial ulcers showed gradual increase over the period between 1997 and 2003 compared with viral keratitis that showed an initial increase between 1997 and 2000 followed by progressive decline till 2003. In 2006 the overall rate of infectious keratitis was lower than that in the retrospective study due to the significant decrease in viral keratitis ($p=0.0003$).

In contrast to viral keratitis, the rate of bacterial corneal ulceration increased from 43.6% in the retrospective study to 58.2% in the prospective study. Contact lens wear was the main risk factor in both studies that increased from 31% in the retrospective study to 45.3% in 2006 with corresponding increase in the annual incidence of lens-related corneal ulcers from 16.2 to 18.2 per 100,000 persons respectively. However, there was no significant difference in the rate of fungal, *Acanthamoeba* and Chlamydial ulcers between the two studies ($p=0.5$). According to the results of our retrospective and prospective studies, an average of 12 days was needed for complete corneal ulcer resolution.

Incidence and annual distribution of different types of infectious corneal ulcers in the retrospective and prospective studies are shown in the given Table 1 and Figure 1.

Discussion

The current study included large number of patients with infectious corneal ulcers who over two different periods attended the eye casualty department at QAH, Portsmouth, one of the busiest hospitals in south England that serves the residents within the boundaries of the town of Portsmouth and the surrounding catchment areas in the county of Hampshire.

This large study is likely to give a realistic and accurate reflection of the exact incidence of infectious corneal ulceration and the related potential risk factors. There are several important factors that make the results of our study a good and reliable indicator of the incidence corneal ulceration in Portsmouth.

Our study took place in a developed country and in a tertiary, highly equipped, teaching and very busy hospital based in the south coast of England and applied on a population with a good level of health awareness and high rate of compliance and attendance rate. Almost 93% of patients completed the follow up in the retrospective and prospective studies. In addition, infectious corneal ulceration is a painful and vision threatening disease that makes patients, pharmacists, opticians, general practitioners and other medical staffing in primary and secondary health care units very cautious towards giving medical advices or prescribing treatment if applicable. This makes sure that almost all patients with corneal ulcers are referred and treated by eye specialists at QAH.

The pre-assessment use of topical antibiotic eye preparations, like Chloramphenicol, was noted in some patients. These were prescribed by general practitioners or given as an over the counter medicine by

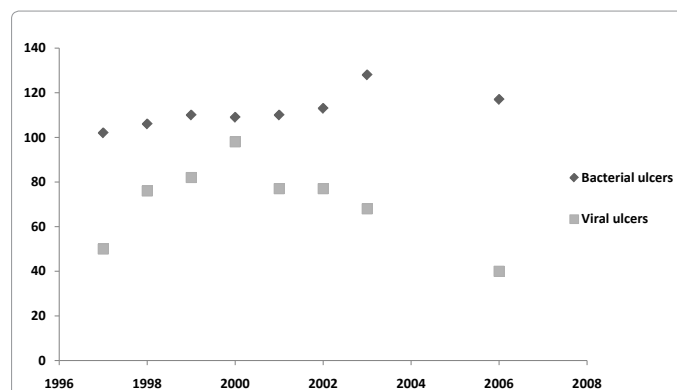


Figure 1: Distribution of bacterial and viral corneal ulcers in the retrospective and prospective studies.

Particulars	Number of patients	Population*	Incidence*	Bacterial ulcers** NO. (%) Incidence	Viral ulcers** NO. (%) Incidence	Fungal ulcers** NO. (%) Incidence	Protozoal ulcers** NO. (%) Incidence	Chlamydial ulcers** NO. (%) Incidence
Retrospective study								
1997	208	488,400	42.6	102 (49) 20.9	50 (24) 10.2	2 (1) 0.4	1 (0.5) 0.2	2 (1) 0.4
1998	257	488,600	52.6	106 (41.2) 21.7	76 (29.6) 15.6	0 (–) ---	3 (1.2) 0.6	2 (0.8) 0.4
1999	264	487,700	54.1	110 (41.7) 22.6	82 (31.1) 16.8	1 (0.4) 0.2	1 (0.4) 0.2	1 (0.4) 0.2
2000	236	487,942	48.4	109 (46.2) 22.3	98 (41.5) 20.1	1 (0.4) 0.2	2 (0.8) 0.4	2 (0.8) 0.4
2001	268	489,000	54.8	110 (41) 22.5	77 (28.7) 15.7	0 (–) ---	2 (0.7) 0.4	2 (0.7) 0.4
2002	272	490,900	55.4	113 (41.5) 23	77 (28.3) 15.7	1 (0.4) 0.2	1 (0.4) 0.2	1 (0.4) 0.2
2003	281	493,200	57.0	128 (45.6) 26	68 (24.2) 13.8	3 (1.1) 0.6	1 (0.4) 0.2	2 (0.7) 0.4
Total	1786	489,391**	52.1	778 (43.6) 22.7	528 (29.6) 15.4	8 (0.4) 0.2	11 (0.6) 0.3	12 (0.7) 0.4
Prospective study								
2006	201	499,100	40.3	117 (58.2) 23.4	40 (19.9) 8.0	3 (1.5) 0.6	1 (0.5) 0.2	2 (1) 0.4

* Population of Portsmouth area includes population of Portsmouth town and the catchment areas served by QAH

* Incidence is given per 100,000 persons of population in every given year

** Some of these values are not pure (mixed with other micro-organisms)

** Average population in 7 years

Table 1: Incidence and annual distribution of infectious corneal ulcers in the retrospective and prospective studies

pharmacists as a routine non-specific first line of treatment of any eye infection. However, the application of topical chloramphenicol would not affect our results even if it is assumed that the causative bacteria were sensitive to it, or the cornea was mildly and tolerably infected that is because of the painful nature of the disease and a long duration of 12 days in average for complete corneal ulcer resolution.

During the retrospective study the annual number of patients with infectious keratitis averaged 255 cases, representing just 3.3% of the total attending an ophthalmic casualty department with different ophthalmic problems. Wong et al. (2003) [19] stated that infective keratitis represented about 2% of annual ophthalmic services in Auckland, New Zealand. In the Hong Kong study [20] 223 patients with different types on infectious keratitis were recruited in a 17 month period, giving an average of 157 patients per year. Also, Bourcier et al. (2003) [3] examined 291 patients with bacterial keratitis in 20 months at the Quinze-Vingts National Centre of Ophthalmology in Paris equating to 175 patients per year.

The relatively low rate of infectious keratitis reported in these studies, compared with the annual rate in our results, could be due to the short period of these studies. Furthermore, in contrast to our study that included all types of infectious keratitis, the French study [3] examined only patients with pure bacterial keratitis and excluded other infections. Also Bourcier et al. (2003) [3] suggested that topical anaesthetics might be responsible for the generalised decrease in the rate of bacteria isolated in their study.

In the London study [21] Tuft and Matheson (2000) studied the profile of 1,312 bacterial isolates over 16 years that accounted for 82 cases per year, but the London data contains tertiary referrals from a large and mobile population, unlike Portsmouth which is a largely fixed population in a combined city and rural area. The annual average in

our study would be lowered to 98 cases per year if only patients with pure bacterial keratitis were included.

Our results showed a 21.2% decline in the rate of infectious corneal ulcers between the retrospective and prospective studies with a decrease in incidence from 52.1 to 40.3 per 100,000 persons per year. This decline in the incidence of infectious keratitis can be attributed to the decrease in the rate of viral keratitis from 29.6% in the retrospective study to 19.9% in the prospective study. Our results showed decrease in the frequency of viral keratitis from 41.5% in 2000 to 24.2% in 2003 to 19.9% in 2006 with a corresponding decrease in the annual incidence of viral keratitis from 20.1 per 100,000 in 2000 to 8 per 100,000 in 2006 (p=0.0003). This decrease in the rate of viral keratitis shows that bacterial keratitis was mainly responsible for the significant upward trend of the overall incidence of infectious keratitis from 42.6 per 100,000 persons in 1997 to its highest level 57 per 100,000 persons in 2003.

A recent decline in the overall incidence of ocular HSV including epithelial and stromal keratitis was recently reported in the USA [17] with an estimated annual incidence of 11.8 per 100,000 people. This decline in incidence was attributed to the increased use of oral prophylactic antiviral medication. However, on contrary to the reported decline in the incidence of HSK in the USA and UK, Labetoulle et al. (2005) [22] reported an overall incidence of HSK in France as high as 31.5 per 100,000 persons per year.

On contrary to the decreased rate of viral keratitis, our results show an increased rate of lens-related corneal ulcers from 31% in the retrospective study to 45.3% in 2006 with a subsequent increase in the rate of bacterial keratitis. Recently in the USA, Jeng et al. [23] reported an increase in the rate of ulcerative keratitis in the population of North California that was attributed to the increasing prevalence of contact lens wear.

The incidence of infectious corneal ulcers given in this study gives an estimate that may be of relevance to the overall incidence of infectious corneal ulcers in the United Kingdom. However, the incidence of infectious corneal ulcers for the whole of the UK could be more accurately detected by multicentre studies or registries. Also further retrospective assessment of the rate of infectious keratitis in Portsmouth centre the three years gap between the introduced retrospective and prospective studies will show the exact change in the pattern of corneal ulceration.

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