

# Bacterial Keratitis in South East of Iran: Major Predisposing Factors and Final Clinical Results

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## Abstract

**Purpose:** Identifying the predisposing factors of the infectious keratitis results in understanding the underlying mechanisms of its expansion and severity that is essential for initiation of optimal empirical antimicrobial therapy. This study identified main predisposing factors of bacterial keratitis in a sample of Iranian population.

**Methods:** Ninety patients with bacterial keratitis were prospectively enrolled. Demographic and clinical features were collected by a face to face interviewing as well as physical examination. Predisposing factors and final outcomes were analyzed.

**Results:** Trauma was the most commonly identified predisposing factor (40.0%), followed by blepharitis and cataract surgery that were observed in 27.8% and 23.3% of patients, respectively. 5.6% of cases were associated with contact lens wear and 4.4% with prior herpetic keratitis. No significant differences were found in overall prevalence of predisposing factors of infectious keratitis between men and women. Fifty-three patients experienced corneal scar and 15.6% of them had corneal neovascularization. Moreover, graft of cornea was programmed in 11.1% of cases and 5.6% of them underwent conjunctival flap.

**Conclusion:** Ocular trauma, followed by surgery and ocular surface diseases are the major predisposing factors for bacterial keratitis. Identification of the appropriate predisposing factors aids in early recognition and treatment of microbial keratitis.

**Keywords:** Bacterium, Infection, Keratitis, Outcome, Prevalence

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## Introduction

Infectious keratitis is one of the most important progressive and destructive disorders of the cornea that is characterized by corneal ulceration, stromal abscess formation, surrounding corneal edema, or anterior segment inflammation. The most common causative bacteria associated with bacterial keratitis are Streptococcus,

Pseudomonas, Enterobacteriaceae (including Klebsiella, Enterobacter, Serratia, and Proteus), and Staphylococcus species.<sup>1-6</sup> The different toxins and enzymes of these bacteria can be produced during corneal infection, contributing to the destruction of corneal substance.<sup>7</sup>

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Besides bacterial pathogens responsible for this ocular infection, some prominent potential causes or predisposing factors for bacterial keratitis have been also known include extended-wear contact lenses, contaminated ocular medications, decreased immunologic defenses secondary to malnutrition, alcoholism, and diabetes, recent corneal disease such as herpetic keratitis and secondary neurotrophic keratopathy, chronic dacryocystitis, as well as using topical corticosteroids.<sup>8</sup> Although association between the type of these predisposing factors and the microbial etiology for keratitis has been identified, this infection may be rarely occurred in normal eyes without any predisposing factors.<sup>9</sup> In addition, incidence and reported risk profiles of bacterial keratitis varies considerably in different population, with less industrialized countries having a significantly lower number of contact lens users and, therefore, significantly fewer contact lens-related infections. Therefore, identifying keratitis-associated predisposing factors result in understanding the underlying pathophysiology and mechanisms of its expansion and severity and can be essential for initiation of optimal empirical antimicrobial therapy with subjective interpretation of presenting clinical features for practicing ophthalmologist. The main goal of the present study was to identify main predisposing factors of bacterial keratitis in our current practice in Kerman, a big city in south east of Iran.

## Methods

In current longitudinal study, all patients with clinically diagnosed infective keratitis presenting at ophthalmology ward of Shafa Hospital in Kerman between April 2007 and September 2009 were consecutively included. Subjects were included if their clinical notes indicated scraping of a new corneal lesion suspected to be bacterial keratitis. Infective keratitis was defined as a suppurative infection of the corneal stroma with an associated overlying epithelial defect and sign of inflammation, characterized by the presence of a white or yellowish stromal infiltrate or infiltrates with an associated epithelial defect, with or without hypopyon.<sup>10,11</sup> Thus, patients with non-bacterial causes of keratitis, and those with no corneal scraping

were excluded. The diagnosis of bacterial keratitis was based on clinical assessment and positive response to anti-bacterial treatment (because notable numbers of samples were negative for culture). This study was approved by the Ethics Committee at Kerman University of Medical Sciences.

Baseline characteristics of patients were collected by a face to face interviewing as well as physical examination. The patients underwent detailed investigations that included: the documentation of the demographic features, education level, history of diabetes, the time interval between the symptoms appearance and hospitalization, previous history of ocular surgery, systemic disorders, injurious agents, the use of traditional eye medications, and therapeutic regimens received prior to the presentation. In the charts, clinical examinations were focused on the following variables: involved eye, location of the lesion (peripheral, mid-peripheral, central or more than one quadrant, lesion depth (deep or superficial), level of anterior chamber reaction (flare, cell, hypopyon), and ocular surface disease (dry eye, blepharitis or meibomian gland dysfunction). Final endpoints of patients' managing were considered as complete improvement, scar formation, corneal vascularization, corneal graft, conjunctival flap, and eye evisceration.

Results were reported as mean±standard deviation (SD) for the quantitative variables and percentages for the categorical variables. The groups were compared using the Mann Whitney U test for the continuous variables and the  $\chi^2$  test (or Fisher's exact test if required) for the categorical variables. P values of 0.05 or less were considered statistically significant. All the statistical analyses were performed using SPSS version 16.0 (SPSS Inc., Chicago, IL, USA) and SAS version 9.1 for Windows (SAS Institute Inc., Cary, NC, USA).

## Results

Of the 140 new cases of corneal ulcers referred to our centre during the study period, 90 consecutive patients were clinically diagnosed as infective non viral keratitis that among them, 55.6% were male. The mean age of all patients was 50.3 years and 13 cases had less than 18 years of age. The

mean age of male patients was 49.0 years, and that of females was 51.9 years ( $P=0.604$ ). Of 90 patients, 3.3% were diabetic. Right eye was involved in 63.3% of participants. The predominant pattern of corneal involvement was central (41.1%), followed by mid-peripheral (30.0%) and 45.6% of subjects had deep corneal lesions. Hypopion as an anterior chamber reaction was detected in less than half of the patients. Underlying ocular surface disorders were found in 78.9% of patients and 31.1% of all subjects had previous history of ocular surgery (Table 1).

An identifiable predisposing factor for keratitis was found in the clinical notes of 87 (96.7%) cases and in the other three patients it remained unknown. Trauma was the most commonly identified predisposing factor (40.0%), followed by blepharitis and cataract surgery that were observed in 27.8% and 23.3% of patients, respectively. 5.6% of cases were associated with contact lens wear and 4.4% with prior herpetic keratitis. No significant differences were found in overall prevalence of predisposing factors of infectious keratitis between men and women (Figure 1). Regarding the prevalence of predisposing factors in different age

subgroups, contact lens-related keratitis and traumatic keratitis were more common in younger patients, whereas keratitis associated with previous ocular surgery or herpetic keratitis was more common in older patients (Figure 2 and Table 4). The group with contact lens-related keratitis had the lowest mean age ( $29.2\pm 11.7$  years) and those with previous ocular surgery had the highest mean age ( $67.4\pm 16.4$  years) (Figure 3).

With respect to the final results of managing infectious keratitis (Table 2), only 5 out of 90 patients completely improved. Fifty three patients experienced corneal scar and 15.6% of them had corneal neovascularization. Moreover, graft of cornea was programmed in 11.1% of cases and 5.6% of them underwent conjunctival flap. There were no differences in final results of managing infectious keratitis between the two genders. Although corneal neovascularization was numerically more documented among patients younger than 50 years and conjunctival flap was numerically more recorded in the elderly, these differences were not significant between the age subgroups (Table 3).

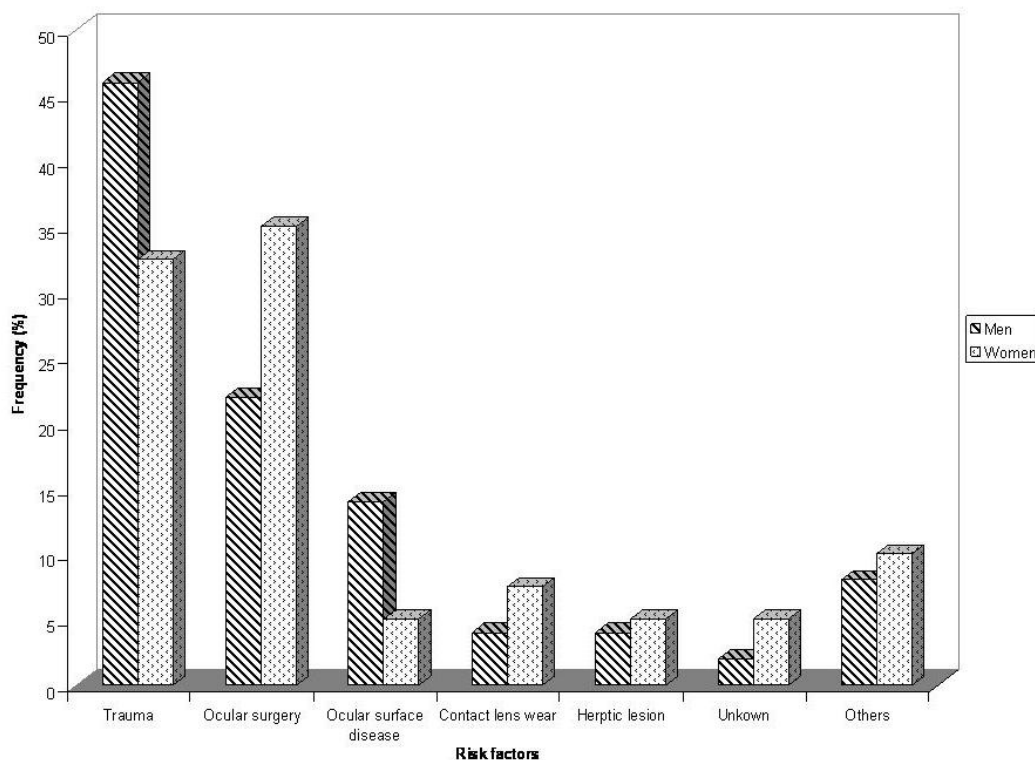


Figure 1. Predisposing factors for infectious keratitis according to sex (All  $P>0.05$ )

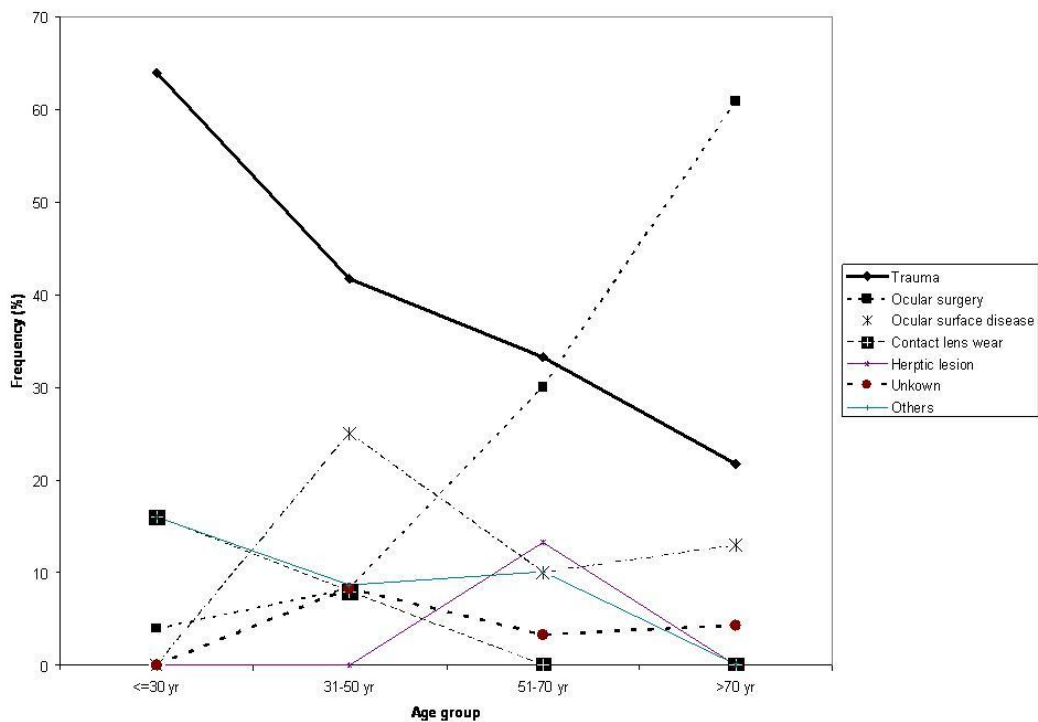


Figure 2. Predisposing factors for infectious keratitis according to age

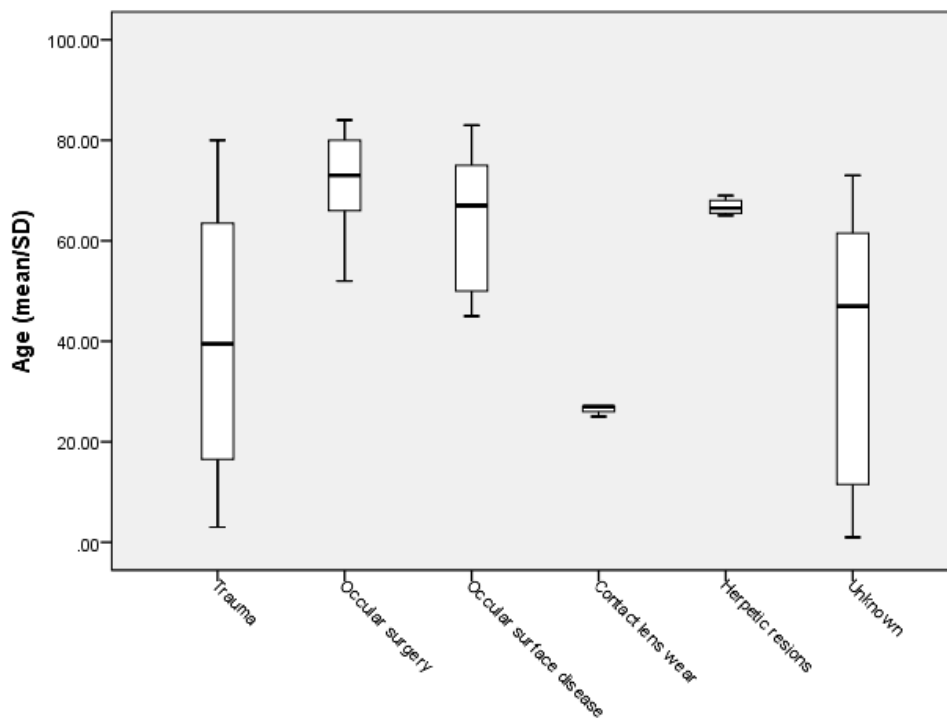


Figure 3. Mean age of patients in different predisposing factor groups for infectious keratitis

**Table 1.** Baseline characteristics and clinical data of study patients

Characteristics	Total (n=90)	Men (n=50)	Women (n=40)	P
Age (yr)	50.3±25.3 *	49.0±24.6	51.9±26.5	0.604
Education level				
Illiterate	63 (70.0)	33 (66.0)	30 (75.0)	
Primary level	18 (20.0)	14 (28.0)	4 (10.0)	0.059
Secondary level	9 (10.0)	3 (6.0)	6 (15.0)	
Diabetes	3 (3.3)	1 (2.0)	2 (5.0)	0.707
Involved eye				
Right eye	57 (63.3)	33 (66.0)	24 (60.0)	0.557
Left eye	33 (36.7)	17 (3.4)	16 (40.0)	
Location of the lesion				
Peripheral	11 (12.2)	4 (8.0)	7 (17.5)	
Mid-peripheral	27 (30.0)	16 (32.0)	11 (27.5)	0.264
Central	37 (41.1)	19 (38.0)	18 (45.0)	
More than one quadrant	15 (16.7)	11 (22.0)	4 (10.0)	
Lesion depth				
Deep	41 (45.6)	20 (40.0)	21 (52.5)	0.237
Superficial	49 (54.4)	30 (60.0)	19 (47.5)	
Anterior chamber reaction				
Hypopion	46 (51.1)	26 (52.0)	20 (50.0)	0.884
Ocular surface disease				
Dry eye	22 (24.4)	13 (26.0)	9 (22.5)	0.701
Blepharitis	25 (27.8)	12 (24.0)	13 (32.5)	0.371
Meibomian gland dysfunction	24 (26.7)	13 (26.0)	11 (27.5)	0.873
History of surgery				
Cataract	21 (23.3)	9 (18.0)	12 (30.0)	0.181
Penetrating Keratoplasty	6 (6.7)	4 (8.0)	2 (5.0)	0.571
Radial Keratotomy	1 (1.1)	0 (0.0)	1 (2.5)	0.261
Time between symptoms appearance and admission (day)	10.1±3.0	10.7±3.2	9.4±3.0	0.722

\* Data are presented as mean±SD or number (%)

**Table 2.** Final results of infectious keratitis

Factor	Frequency (%)
Scar	53 (58.9)
Cornea vascularization	13 (14.4)
Cornea graft	10 (11.1)
Conjunctive flap	5 (5.6)
Improvement	5 (5.6)
VLE	3 (3.3)
Eye evisceration	1 (1.1)

VLE: Visual loss eye  
Data are presented as number (%)

**Table 3.** Final outcome of infectious keratitis in different age subgroups

Factor	<=30 yr (%)	31-50 yr (%)	51-70 yr (%)	>70 yr (%)
Scar	64.0	66.7	60.0	47.8
Cornea vascularization	12.0	8.3	0.0	4.3
Cornea graft	8.0	16.7	10.0	13.0
Conjunctive flap	4.0	0.0	10.0	4.3
Improvement	12.0	8.3	0.0	4.3
VLE	0.0	0.0	10.0	0.0
Eye evisceration	0.0	0.0	0.0	4.3

VLE: Visual loss eye

**Table 4.** Predisposing factors for infectious keratitis in different age subgroups

Item	<=30 yr (%)	31-50 yr (%)	51-70 yr (%)	>70 yr (%)
Trauma	64.0	41.7	33.3	21.7
Ocular surgery	4.0	8.3	30.0	60.9
Ocular surface disease	0.0	25.0	10.0	13.0
Contact lens wear	16.0	8.0	0.0	0.0
Herpetic lesion	0.0	0.0	13.3	0.0
Others	16.0	17.0	13.4	4.4

## Discussion

A few published studies are available on the frequency of predisposing factors for bacterial keratitis and on the demographic characteristics of patients. Few studies have also reported on clinical differences between the two genders and also between the elderly and younger with bacterial keratitis. Moreover, microorganisms implicated in this ocular infection may differ from one geographic area to another<sup>12-14</sup> which demands both isolation of pathogens and identification of predisposing factors. In addition, lesions can result in important ophthalmologic problems responsible for visual disability or blindness particularly, in developing countries that can be frequently related to environmental predisposing factors.<sup>15,16</sup> Therefore, we tried to identify main predisposing factors of keratitis and also compare them between the different age subgroups and the two genders. The actual prevalence of infectious keratitis in our patients' population has been unknown and therefore determining the prevalence and sex and age distribution of infectious keratitis in our population can be very valuable for

optimizing therapeutic approaches in these patients.

In our survey, an identifiable predisposing factor for keratitis was found in the clinical notes of 96.7% cases and thus in 3.3% of them remained unknown. Age-independent similar studies identified factors in 88-94% of patients with microbial keratitis<sup>3,17</sup> that the wide reported unknown cases can be due to the inappropriate diagnostic technical approaches and/or unsuitable managing plans of these patients specially in the rural regions of developing countries.

Regarding the predisposing factors of bacterial keratitis in our patients, organic material trauma was the most frequent identified factor with the overall prevalence of 40.0%. The reported prevalence of ocular trauma as a common predisposing factor for keratitis has wide spectrum in different nations. In a similar study by Gopinathan et al in India, the patients with ocular trauma might be 5.33 times more likely to develop microbial keratitis.<sup>17</sup> In Keay et al study in Australia, ocular trauma was the most commonly identified predisposing factor in 36.4% of

referred subjects.<sup>3</sup> In another study by Green in Australia, predisposing role of trauma was observed only in 16% of admitted patients, while contact lens wear was the most common predisposing factor for bacterial keratitis with the prevalence rate of 22.0%.<sup>18</sup> This factor in another study among American children who were younger than 16 years was found in 21.2% of cases.<sup>19</sup> Trauma to the eye can cause ulceration of the corneal epithelium; once the epithelium is breached, the corneal stroma and deeper part of the cornea are prone to become secondarily infected by bacteria. This relationship between trauma and corneal complications was confirmed in different recent researches.<sup>20-25</sup>

In our study, traumatic keratitis was more common in younger patients; however its prevalence in older subjects was notably high. The predominance of corneal trauma-related keratitis even in the elderly in similar developing nations might be explained by the fact that many older adults still live in undeveloped rural areas, as previous reports have indicated,<sup>26,27</sup> but this different prevalence could not be revealed between the two sexes.

In the present study, ocular surgery specially cataract was the second common predisposing factor for bacterial keratitis in Iranians. Ocular surgeries were mainly consisting of cataract and penetrating keratoplasty, followed by radial keratotomy that had been rarely performed in our samples. With the increasing incidence of refractive surgeries such as laser in situ keratomileusis (LASIK) and photorefractive keratectomy (PRK),<sup>32,33</sup> corneal surgery has been identified as an important predisposing factor for infectious keratitis. However, infectious keratitis rarely occurs following PRK.<sup>30</sup>

In our study, only 5.6% of cases were associated with contact lens wear that was predominantly reported in younger group. Contact lens wear is relatively common in younger patients and may partially account for the high incidence of Gram-negative bacterial infection.<sup>26,27</sup> Differing from other studies,<sup>9,26</sup> we observed a low incidence of contact lens wear as a predisposing factor for infectious keratitis. This low incidence of contact lens wear as a predisposing factor to infectious keratitis may be explained by the low socioeconomic levels of patients referred to this hospital.

Our study confirms that major differences in types of predisposing factors exist between older and younger patients and this age profile in our patients is comparable with previous reports. Similar to other studies, contact lens wear remains the most common predisposing factor among younger patients,<sup>1,3,9,26</sup> whereas among the elderly, the most prevalent predisposing factor was previous ocular surgery.<sup>1,2</sup> Therefore, preventive approaches should be programmed based on identifying common predisposing factors of bacterial keratitis in each special age subgroups.

Finally, we should acknowledge that the epidemiology of bacterial keratitis and predisposing factors reported in this study is specific to the city and the area of Kerman, Iran and therefore further studies on other population in different regions are recommended.

## Conclusion

In conclusion, our study suggests that the main predisposing factors for bacterial keratitis include ocular trauma, surgery and ocular surface disease. Thus, Identification of these factors aids in early recognition and treatment of microbial keratitis.

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