Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/2738
DOI URL: http://dx.doi.org/10.21474/IJAR01/2738

*RESEARCH ARTICLE*

# EPIDEMIOLOGY AND ETIOLOGY OF CORNEAL ULCER WORLDWIDE SYSTEMATIC REVIEW

**Lama H. Saleh.**

## Manuscript Info

***Manuscript History***

Received: 15 November 2016
Final Accepted: 17 December 2016
Published: January 2017

## Abstract

**Background:** Infectious keratitis (corneal ulcer) is defined as a corneal characterized as a corneal inflammatory process connected with an overlying epithelial damage and it's a vision-threatening medical condition displaying in all age population and either sex that changes in morbidity rate through worldwide, its caused by bacteria, fungi, protozoa or viruses, and presents with pain, photophobia and redness. If left untreated, apart from scar formation, it can lead to endophthalmitis and even corneal perforation and blindness.

**Objectives:** The aims of this corneal ulceration study was therefore to establish the incidence of different types infectious corneal ulcers and to discuss the evidence based treatment that were approved in different world wide studies.

**Methodology:**we conducted a systematic review study that performed through Comprehensive literature search was performed in MEDLINE/PubMed and Cochrane Central Register of Controlled Trials using combinations of the following search terms: "corneal diseases, corneal keratitis" or "corneal ulcer. Epidemiology, Etiology, treatment" our search was ended on 14th of July 2016.

**Conclusion:** Corneal Keratitis is an important cause of ophthalmic disorders worldwide. Most common causes of corneal ulceration include including the infectious keratitis which is caused by bacterial, fungal, viral, and protozoan, the diagnosis of which is made on clinical examination aided by microbiological demonstration in smears or cultures from corneal tissues.



## Introduction: -

Corneal ulceration is defined as a corneal infiltrate associated with an overlying epithelial defect and it's a vision-threatening medical condition presenting in all age groups and either sex that varies in morbidity worldwide. It might resolve with no medical intervention, advancement to aperture and its resultant outcomes, or leave behind an opacity which if focal may prompt loss of vision. Variety in occurrence of infectious keratitis is a multi-factorial issue that includes a tight mix of different factors, for example, geological and other area related elements[(1)], degree of development of the country concerned, the predominant predisposing factors and the type of infection commonly present in this community [(2)]. However, varieties in frequency of corneal keratitis have been accounted for in various keratitis trails in various nations despite the fact that these were comparative in the level of development, topographical area, and the most common sort of corneal contamination and related inclining components. Also, within the same nation, France for instance, varieties have been accounted for in the rate of serious types of irresistible keratitis that required healing facility confirmation [(3-5)].

**Corresponding Author:-Lama H. Saleh.**

According to some studies it is generally acknowledged that bacterial and fungal keratitis have far higher rate in the developing world than that in the developed world [22,23]. 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 [24,25]. However, predominance of bacterial [3] and fungal [26,27,28] keratitis in developed countries has been reported.

**Objectives: -**

The aims of this corneal ulceration study was therefore to establish the incidence of different types infectious corneal ulcers and to discuss the evidence based treatment that were approved in different world wide studies. And to highlight the most common causes of corneal ulcers in different populations. In contrast this review was aimed to give the chance for healthcare professional and patients to understand the epidemiology, predisposing factors, etiology and the outcome of management of corneal ulcers.

## Methodology: -

We conducted a systemic review study that performed through Comprehensive literature search was performed in MEDLINE/PubMed and Cochrane Central Register of Controlled Trials according to the validated methods of the Preferred Reporting Items for Systematic Reviews (RRISR) [40](using combinations of the following search terms: "corneal diseases, corneal keratitis, Corneal Infiltrate, Corneal Inflammations, Microbial Keratitis" or "corneal ulcer. Epidemiology, Etiology, treatment" our search was ended on 14th of July 2016. Extracted data from individual studies were summarized according to the main objects that our study is concerning about Epidemiology and Etiology of corneal ulcer.

This search was limited to English languages studies, we excluded all case reports, comments, reports, and we included reviews, cross sectional studies and all randomized control studies which met the criteria of our search which are every study discussing the incidence and causes of corneal ulcers from different populations worldwide published in English language.

**Data collection: -**

Using a structured data abstraction form, different authors extracted the data from the included studies, and another independent author checked the extracted data. Disagreements were resolved through discussion and if necessary by involving another independent author.

## Results and Discussion: -

Our search identified 89 studies concerning the corneal ulceration and we have and included only12 studies for the epidemiology concerning corneal ulceration, and 19 studies included in the Etiology of corneal ulcer.

**Epidemiology of corneal ulceration: -**

Corneal ulceration was not considered as imperative reason for corneal visual deficiency. Both injury and ulceration are normally monocular and influenced people, consequently, not portrayed as thoroughly visual impairment but rather just as outwardly incapacitated. Nonetheless, as general health programs have turned out to be more compelling in lessening the predominance of conventional reasons for corneal visual impairment, for example, corneal ulceration have turned out to be moderately more critical. In 1992, Thylefors et al, attracted regard for the way that injury is regularly the most imperative reason for corneal ulcer and one-sided loss of vision in creating nations and that up to 5% of all respective visual deficiency after corneal ulcer is an immediate consequence of injury [6]. The implication is that well over half a million people in the world are blind as a result of eye injuries [7]. A careful analysis of the world literature by Negrel & Thylefors in 1998 brought to light a global epidemic of ocular trauma with some 55 million eye injuries occurring annually, of which 750 000 cases required hospitalization and 200 000 were open-globe injuries [8]. They further estimated that approximately 1.6 million people were blind from their injuries, 2.3 million had bilateral low vision, and 19 million were unilaterally blind or had low vision. Even though ocular trauma is a global problem, the burden of blindness from eye injuries falls most heavily on developing countries, especially those where war and civic unrest have left a legacy of eye trauma from weapons such as land mines [9]. A country-wide population-based survey in Nepal a country with a peaceful history reported that trauma was responsible for 7.7% of all monocular blindness [10]. A more recent population-based prospective study in Bhaktapur District in Kathmandu valley, Nepal, revealed that the annual incidence of ocular injury is 1788 per 100 000 people, with 789 of the injuries due to corneal abrasions [11]. In other words, 1.8% of the residents of Bhaktapur

District experience some form of ocular injury every year. In Nepal and other developing countries, injuries are usually associated with agricultural work, but a much higher rate of ocular trauma can occur in specialized situations, such as foundries: an 11% eye-injury rate was reported in foundry workers in Saudi Arabia [12]. Corneal ulceration in developing countries has only recently been recognized as a ''silent epidemic'' [13]. Gonzales et al. found that the annual incidence of corneal ulceration in Madurai District in South India was 113 per 100 000 people, see figure 1 [14], 10 times the annual incidence of 11 per 100 000 reported from Olmsted County, Minnesota, in the United States of America [15]. By applying the 1993 corneal ulcer incidence rate in Madurai District to all of India, there are an estimated 840 000 people a year in the country who develop an ulcer. This figure is 30 times the number of corneal ulcers seen in the United States [14]. Extrapolating the Indian estimates further to the rest of Africa and Asia, the number of corneal ulcers occurring annually in the developing world quickly approaches 1.5–2 million, and the actual number is probably greater. Invariably corneal blindness is the end result in the majority of these infections; outcomes may be even more disastrous such as corneal perforation, endophthalmitis, or phthisis. In a prospective population-based study by Upadhyay et al.2001 in Bhaktapur District, Nepal, the annual incidence of corneal ulceration was found to be 799 per 100 000 people [11].

Glynn RJ et al 1992, in his study showed that the annualized incidence of ulcerative keratitis among aphakic persons using contact lenses was estimated to be 52 cases per 10,000 aphakic contact lens wearers (95% confidence interval (CI), 31.1 to 86.9). The risk of ulcerative keratitis varied substantially by lens use, with extended wear having an estimated sevenfold greater risk relative to daily wear (95% CI, 1.6 to 30.2) [16].

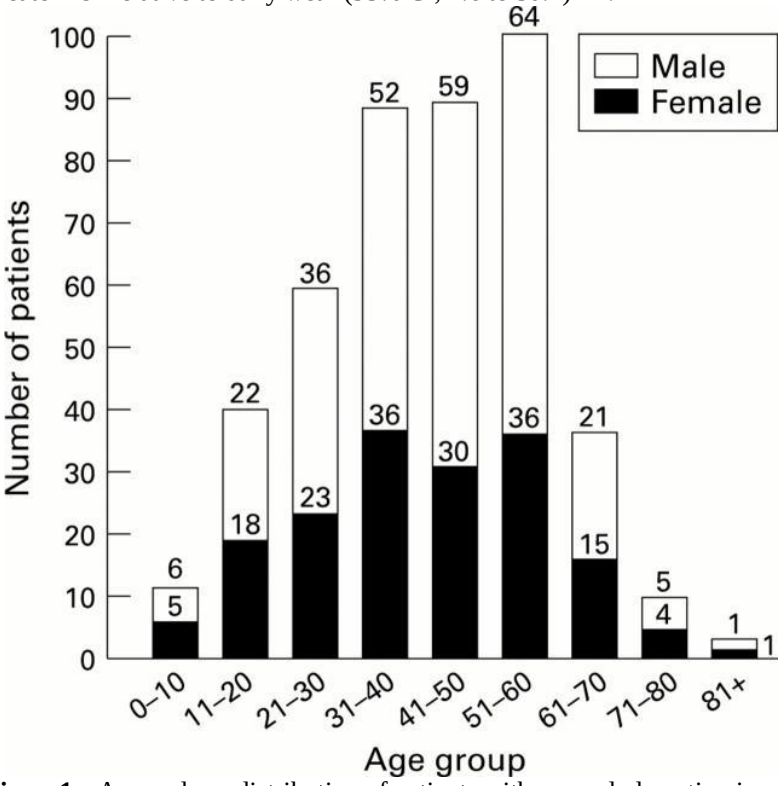


**Figure1: -**Age and sex distribution of patients with corneal ulceration in south India.

A recent trail that was targeting population of 1 093 210 patients in Northern California performed by (Jeng BH et al. 2010), found that out of this large population number 302 developed ulcerative keratitis. The incidence of ulcerative keratitis was 27.6 per 100 000 person-years (95% confidence interval, 24.6-30.9). The incidence of corneal ulceration in contact lens wearers was 130.4 per 100 000 person-years (95% confidence interval, 111.3-151.7), with an adjusted relative risk of 9.31 (7.42-11.7; $P < .001$) compared with non-contact lens wearers, who had an incidence of ulcerative keratitis of 14.0 per 100 000 person-years (11.7-16.6). Seven of 2944 people known to be infected with human immunodeficiency virus developed ulcerative keratitis, with 5 being contact lens wearers. The incidence of ulcerative keratitis in human immunodeficiency virus-positive patients was 238.1 per 100 000 person-years. [18]

**Etiology: -**
The regular danger variables for corneal keratitis incorporate visual injury, contact lens wear, recent visual surgery, previous visual surface disease, dry eyes, lid deformity, corneal sensation impairment, chronic use of topical steroids and systemic immunosuppression [32,33,24].

**Microbial keratitis (infectious corneal ulceration): -**
Microbial keratitis is an infection of the cornea that is associated with a risk of permanent visual impairment [3,24,25,27,29]. It can be caused by bacteria, virus, fungus, protozoa and parasites.

Wong et al. (2003) [29] stated that infective keratitis represented about 2% of annual ophthalmic services in Auckland, New Zealand. In the Hong Kong study [30] 223 patients with different types on infectious keratitis were recruited in a 17-month period, giving an average of 157 patients per year.

A study that was conducted by T Bourcier et al, 2003 in Quinze-Vingts National Center of Ophthalmology, Paris, France included 300 cases, showed that in 207 eyes (68.2%), bacteria were identified from the corneal cultures. the hospital culture grew an identifiable organism in 58% of cases. Gram positive bacteria were predominant (83% of all positive cultures), mainly coagulase negative *Staphylococcus* species; Gram negative bacteria (17%) were mostly *Pseudomonas* and *Serratia* species. Polybacterial infection was noted in six cases (2%). Twenty-eight per cent of culture positive isolates were detected on smears[17].

In contact Lenses wearers group, 63.3% of the corneal scrapings were positive. Thirty per cent of isolated bacteria were Gram negative, mostly *Pseudomonas aeruginosa*. Contact lens and/or storage cases cultures were performed in 67 cases (Table 1). An organism was identified in 83.6% (56) of cases. Ninety-seven per cent of the organisms were Gram negative bacteria. The bacteria isolated were similar to the organism recovered by corneal scraping in 14 cases [17].

**Table 1: -** Contact lenses bacteriological study, T Bourcier et al, 2003 [17]

| | |
|---|---|
| Gram negative bacteria | |
| *Pseudomonas aeruginosa* | 22 |
| *Serratia marcescens* | 18 |
| *Serratia liquefasciens* | 11 |
| *Klebsiella pneumoniae* | 3 |
| *Klebsiella oxytoca* | 8 |
| *Stenotrophomonas maltophilia* | 7 |
| *Alcaligenes xylosidans* | 5 |
| *Enterobacter cloacae* | 3 |
| *Shewanella putrefasciens* | 2 |
| Others | 11 |
| Gram positive bacteria | |
| *Staphylococcus epidermidis* | 3 |
| Negative | 11 |
| Total | 104 |

The spectrum of micro-organisms responsible for corneal ulceration varies according to geographical location. a very old reports from the northern parts of the United States of America show predominantly Gram-positive organisms[19]. While the southern parts show a striking number of fungal and Gram-negative isolates [20]. A study from London in 1989 also showed predominantly Gram-positive isolates. Variations such as these are probably worldwide.

Over the period of 7 years (Ibrahim YW et al 2012) have conducted retrospective study that detected linear trend pathogens causing corneal ulcers which 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 ($p=0.0003$) as it shows in Table 2 [21].

**Table 2: -** Incidence and annual distribution of infectious corneal ulcers in the retrospective and prospective studies, (Ibrahim YW et al 2012) [21]

| 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

(Keshav et al. 2008) performed his study among 188 patients treated for corneal ulcers in Sur regional hospital in Oman through duration of 6 years. When microbiological isolation was evaluated it was found that in 76 patients (43.18%) bacteria/fungi. Among the isolates, 9 cases (11.84%) were fungi and the rest (88.26%) were bacteria. Of the bacterial isolates, pseudomonas was found in 35 cases (53.84%), staphylococci were found in 13 cases (20%), streptococcus pneumonia was found in 12 cases (18.46%), streptococci were found in 2 cases (3%) and klebsiella was found in 5 patients (7.69%) [31]. figure 2

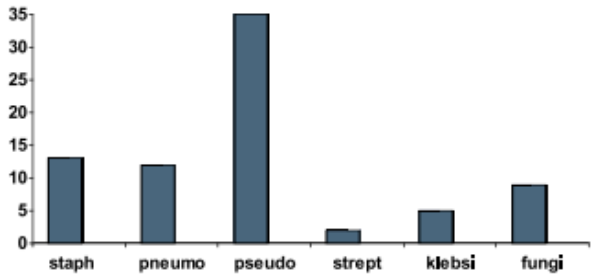


**Figure 2: -** Shows the proportion of patients with specific microbial isolates in positive cultures (Keshav et al. 2008) [31]

(Shojaet al, 2004) conducted a trail in Shahid Sadoughi Hospital, School of Medicine, Yazd, Iran, identified 80 cases of microbial keratitis from March 1999 to March 2001. And they found32 patients (40%) had positive cultures, 22 of which were gram-positive. The most common strains were Staphylococcus epidermidis, Staphylococcus aureus and Streptococcus pneumonia and in the gram-negative group, pseudomonas was the most common isolate. In 21% of gram-negative and 13% of gram-positive cultures, the patients had used one or more topical antibiotics before admission. Keratitis caused by pseudomonas strain (10 cases) had the largest diameter, the highest mean number of days of hospital stay, and the poorest final VA. Two of the 5 patients with fungal keratitis, developed corneal perforation [35]. Table 3

**Table 3: -**Distribution of the patients according to age and predisposing factors (Shoja et al, 2004) [35]

| Age groups | Predisposing factors | | | | | |
|---|---|---|---|---|---|---|
| | Trauma | Ocular disease | Previous ocular surgery | Contact lens | Systemic disease | Total |
| 0-20 | 12 (66.7) | 3 (16.7) | 1 (5.5) | 2 (11.1) | 0 (-) | 18 |
| 20-50 | 11 (40.8) | 7 (25.9) | 3 (11.1) | 6 (22.2) | 0 (-) | 27 |
| 50-80 | 9 (25.7) | 18 (51.5) | 4 (11.4) | 0 (-) | 4 (11.4) | 35 |

Data are given as number (percentage)

*Non infectious corneal ulcer (Idiopathic keratitis)*

**Peripheral ulcerative keratitis:-**

according to (Mondino BJet al, 1988) Noninfectious/inflammatory keratitis can be subdivided into micro-ulcerative and macro-ulcerative. Micro-ulcerative peripheral keratitis includes marginal catarrhal ulcer, phlyctenulosis and peripheral rosacea keratitis. Macro-ulcerative peripheral keratitis is generally a manifestation of systemic, immune-mediated disease. Peripheral ulcerative keratitis has been associated with nearly all connective tissue diseases or vasculitis. However, the most common entities associated with are rheumatoid arthritis, Wegener's granulomatosis and polyarthritisnodosa. When associated with systemic disease, Peripheral ulcerative keratitis represents a local vasculitis affecting the limbal arcades. Circulating immune complexes deposit in the limbal vessels inciting local inflammation, which include diffusion of immune complexes, components of complement system, and inflammatory cells into the peripheral cornea. Loss of stromal collagen leading to descemetocele formation has been reported [(36)].

**Corneal ulcer following the use of non-steroidal anti-inflammatory agents: -**

Topical non-steroidal anti-inflammatory drugs have been reported to be the cause of corneal melting and perforation [(37)]. Impairment of wound healing, neurotrophic effect and activation of matrix metalloproteinase are responsible for the melting. (Gokhale *et al.*2010), have reported a case of diclofenac-induced acute corneal melt after collagen cross linking [(38)]. The surrounding cornea of perforation showed regenerative changes with large epithelial cells. The adjacent stroma showed edema, keratocyte loss, myofibriblastic transformation of keratocytes, and few neutrophils and round cell infiltrate this was according to study by (O'Brien et al, 2001) [(39)].

## Conclusion:-

Corneal Keratitis is an important reason for ocular morbidity worldwide. A substantial part of the standard etiology for corneal keratitis integrate bacterial, fungal, viral, and protozoan, the analysis which is made on scientific assessment supported by microbiological presentation in smears or cultures from corneal tissues. Non-infectious keratitis can likewise be seen in a number of conditions where swelling happens in the cornea due to other etiologies, causing corneal vascularization, scarring and visual loss.

## References: -


1. Ibrahim YW, Boase DL, Cree IA (2007) Factors affecting the epidemiology of Acanthamoeba keratitis. Ophthalmic Epidemiology 14: 53-60.
2. Bharathi MJ, Ramakrishnan R, Meenakshi R, Shivakumar C, Raj DL (2009) Analysis of the risk factors predisposing to fungal, bacterial & Acanthamoeba keratitis in south India. Indian J Med Res 130: 749-757.
3. Bourcier T, Thomas F, Borderie V, Chaumeil C, Laroche L (2003) Bacterial keratitis: predisposing factors, clinical and microbiological review of 300 cases. Br J Ophthalmology 87: 834-838.
4. Kerautret J, Raobela L, Colin J (2006) Serious bacterial keratitis: a retrospectiveclinical and microbiological study. J Fr Ophtalmol 29: 883-888.
5. Ancele E, Lequeux L, Fournie P, Chapotot E, Douat J, et al. (2009) Severe bacterial keratitis. A clinical, epidemiologic, and microbiologic study. J Fr Ophtalmol 32: 558-565.
6. Thylefors B. Epidemiological patterns of ocular trauma. Australian and New Zealand Journal of Ophthalmology, 1992, 20: 95–98.
7. Anderson JDC, Foster A. Ocular trauma. Tropical Doctor, 1989, 19: 35–40.
8. Negrel AD, Thylefors B. The global impact of eye injuries. Ophthalmic Epidemiology, 1998, 5: 143–167.
9. Jackson H. Bilateral blindness due to trauma in Cambodia. Eye, 1996, 10: 517–520.
10. Brilliant LB et al. Epidemiology of blindness in Nepal. Bulletin of the World Health Organization, 1985, 63: 375–386.
11. Upadhyay M et al. The Bhaktapur Eye Study: Ocular trauma and antibiotic prophylaxis for the prevention of corneal ulceration in Nepal. British Journal of Ophthalmology, 2001 (in press).
12. Ballal SG. Ocular trauma in an iron forging industry in the eastern province, Saudi Arabia. Occupational Medicine, London, 1997, 47: 77–80.
13. Whitcher JP, Srinivasan. Corneal ulceration in the developing world — a silent epidemic. British Journal of Ophthalmology, 1997, 81: 622–623.
14. Gonzales CA et al. Incidence of corneal ulceration in Madurai District, South India. Ophthalmic Epidemiology, 1996, 3: 159–166.

15. Erie JC et al. Incidence of ulcerative keratitis in a defined population from 1950 through 1988. Archives of Ophthalmology, 1993, 111: 1665–1671.
16. Glynn RJ, Schein OD, Seddon JM, Poggio EC, Good fellow JR, Scardino VA, Shannon MJ, Kenyon KR. The incidence of ulcerative keratitis among aphakic contact lens wearers in New England. Arch Ophthalmology. 1991;109(1):104-107. doi:10.1001/archopht.1991.01080010106041.
17. T Bourcier, F Thomas, V Borderie, C Chaumeil, and L Laroche. Bacterial keratitis: predisposing factors, clinical and microbiological review of 300 cases. Br J Ophthalmology. 2003 Jul; 87(7): 834–838.
18. Jeng BH, Gritz DC, Kumar AB, Holsclaw DS, Porco TC, Smith SD, Whitcher JP, Margolis TP, Wong IG. Epidemiology of ulcerative keratitis in Northern California. Arch Ophthalmology. 2010 Aug;128(8):1022-8. doi: 10.1001/archophthalmol.2010.144.
19. Liesegang TJ, Forster RK. Spectrum of microbial keratitis in South Florida. AmJ Ophthalmology 1980; 90: 38-47.
20. Thomas PA. Keratomycosis (mycotic keratitis). Bailliire's dinical tropical medicine and communicable diseases. London: Bailliere, 1989; 4: 269-86.
21. Ibrahim YW, Boase DL, Cree IA (2012) Incidence of Infectious Corneal Ulcers, Portsmouth Study, UK. J Clinic Experiment Ophthalmology S6:001. doi:10.4172/2155-9570.S6-001.
22. Poole TR, Hunter DL, Maliwa EM, Ramsay AR (2002) Etiology of microbial keratitis in northern Tanzania. Br J Ophthalmology 86: 941–942.
23. Upadhyay MP, Srinivasan M, Whitcher JP (2007) Microbial keratitis in the developing world: does prevention work? Int Ophthalmology Clin 47: 17-25.
24. Liesegang TJ (1989) Epidemiology of ocular herpes simplex. Natural history inRochester, Minn, 1950 through 1982. Arch Ophthalmology 107: 1160-1165.
25. Liesegang TJ (2001) Herpes simplex virus epidemiology and ocular importance. Cornea 20: 1-13.
26. Liesegang TJ, Forster RK (1980) Spectrum of microbial keratitis in South Florida. Am J Ophthalmology 90: 38–47.
27. Kaufmann C, Frueh BE, Messerli J, Bernauer W, Thiel MA (2008) Contact lens-associated fusarium keratitis in Switzerland. Klin Monbl Augenheilkd 225: 418-421.
28. Proenca-Pina J, Ssi Yan Kai I, Bourcier T, Fabre M, Offret H, et al. (2010) Fusarium keratitis and endophthalmitis associated with lens contact wear. Int Ophthalmology 30: 103-107
29. Wong T, Ormonde S, Gamble G, McGhee CN (2003) Severe infective keratitisleading to hospital admission in New Zealand. Br J Ophthalmology 87: 1103-1108.
30. Lam DS, Houang E, Fan DS, Lyon D, Seal D, et al. (2002) Incidence and risk factors for microbial keratitis in Hong Kong: comparison with Europe and North America. Eye 16: 608-618.
31. Keshav BR, Zacheria G., Ideculla T., Bhat V., Joseph M.Epidemiological Characteristics of Corneal ulcers in south sharqiya Region. Oman Medical Journal 2008, Volume 23, Issue 1, January 2008.
32. Green M, Apel A, Stapleton F. Risk factors and causative organisms in microbial keratitis. Cornea.2008;3:22–27.
33. Saeed A, D'Arcy F, Stack J, Collum LM, Power W, Beatty S. Risk factors, microbiological findings, and clinical outcomes in cases of microbial keratitis admitted to a tertiary referral center in Ireland.Cornea. 2009;3:285–292.
34. Jeng BH, Gritz DC, Kumar AB, Holsclaw DS, Porco TC, SmithSD WJP, Margolis TP, Wong IG. Epidemiology of ulcerative keratitis in Northern California. Arch Ophthalmology. 2010;3:1022–1028.
35. M. R. Shoja and M. Manaviat .Epidemiology and outcome of corneal ulcer in Yazd Shaghid Sadoughi Hospital. Acta Medica Iranica, 42(2): 136-141; 2004.
36. Mondino BJ. Inflammatory diseases of the peripheral cornea. Ophthalmology. 1988;95:463–72.
37. Guidera AC, Luchs JI, Udell IJ. Keratitis, ulceration, and perforation associated with topical nonsteroidal anti-inflammatory drugs. Ophthalmology. 2001;108:936–44.
38. Gokhale NS, Vemuganti GK. Diclofenac-induced acute corneal melt after collagen crosslinking for keratoconus. Cornea. 2010;29:117–9.
39. O'Brien TP, Li QJ, Sauerburger F, Reviglio VE, Rana T, Ashraf MF. The role of matrix metalloproteinases in ulcerative keratolysis associated with perioperative diclofenac use. Ophthalmology.2001;108:656–9.
40. Moher D, Liberati A, Tetzlaff J, Altman DG. PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int J Surg 2010;8:336-41.