Factors associated with poor presenting vision among patients with microbial keratitis In Uganda

Arunga S[1,2], Atto G[2] , Ayebazibwe B[3], Onyango J[2], Macleod D[4], Hu VH[1], Burton MJ[1]

[1]International Centre for Eye Health, London School of Hygiene & Tropical Medicine, UK
[2]Department of Ophthalmology, Mbarara University of Science and Technology, Uganda
[3]Ruharo Eye Centre, Ruharo Mission Hospital, Mbarara, Uganda
[4]Tropical Epidemiology Group, London School of Hygiene & Tropical Medicine, UK

Corresponding author: Dr Simon Arunga, International Centre for Eye Health, Clinical Research Department, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, United Kingdom. Email: Simon.Arunga@lshtm.ac.uk

ABSTRACT

Objective: To determine factors associated with poor presenting vision among patients with microbial keratitis in Uganda.
Design: Retrospective audit study.
Methods: This was a study of patients presenting with microbial keratitis at the two main eye units in Southern Uganda in the year 2015. Information on time to presentation, treatment history, use of traditional eye medicine, trauma and presenting final visual acuity was collected. Factors associated with a poor presenting vision in a regression model were analysed.
Results: There were 273 cases during the year 2015. The median presentation time was 7 days from onset (IQR 2-21, total range 0-366 days). Trauma was reported in 59/88 (67%) patients and 69/162 (43%) reported using traditional eye medicine. Visual acuity was reported in only 216/273 cases at presention. Visual acuity at presentation of less than 6/60 (severe visual impairment) was strongly associated with the use of traditional eye medicine (OR 5.13, 95%CI 2.17–12.1, p=0.001) and distance from the eye hospital (OR 1.02, 95% CI 1.01-1.03, p=0.002).
Conclusion: This audit highlighted the role of use of traditional eye medicine and long distance from the eye hospital in contributing to poor presentation among patients with microbial keratitis in Uganda.

Key words: Microbial keratitis, Bacterial keratitis, Fungal keratitis, Keratitis, Traditional eye medicine, Uganda

INTRODUCTION

Microbial Keratitis (MK) can be caused by a range of pathogens including bacteria, viruses, protozoa and fungi. MK frequently leads to sight-loss from dense corneal scarring, or even loss of the eye, especially when the infection is severe and/or appropriate treatment is delayed[1]. MK has been described as a "silent epidemic", which leads to substantial morbidity, related to blindness and other consequences such as pain and stigma[2]. It is the leading cause of unilateral blindness after cataract in tropical regions and is responsible for about 2 million cases of monocular blindness per year[3].

A good outcome depends on early appropriate treatment, correct identification of the causative organism, and careful follow-up[4,5]. In Low and Middle-Income Countries (LMIC), MK presents major challenges. Majority of patients present with advanced disease when little can be done. Ultimately, outcomes tend to be poor[6,7]. Outcome data from Sub Saharan Africa (SSA) have reported overall cure rates with and without scarring of about 50% and the majority of patients end up with vision of less than 6/60[6, 8-13].

The purpose of our audit was to determine factors associated with poor presentation among patients with MK in rural South-Western Region of Uganda.

MATERIALS AND METHODS

We conducted a retrospective audit of all patients with MK that presented to Ruharo Eye Centre (REC) and Mbarara University and Referral Hospital Eye Centre (MURHEC) during the year 2015. MURHEC is a government owned tertiary eye unit establishedin 2013. It provides mostly free services and sees about 6,000 - 10,000 patients/year. REC is a church-based fee-paying tertiary eye hospital founded in the 1960s. It offers eye care services to about 20,000 - 25,000 patients/year. Both hospitals are located in Mbarara Municipality, South-Western Region, Uganda, approximately four hours drive from Kampala. The two units are about 5km apart and work closely together.

This study adhered to the tenets of Declaration of Helsinki. It was approved by the London School of Hygiene & Tropical Medicine Ethics Committee (Ref:10647). It was approved as an audit study by both MURHEC and REC. All data were anonymized after extraction from clinical notes.

The study included all patients who were recorded to have a clinical diagnosis of either clinically diagnosed fungal or bacterial keratitis presenting between 1st January and 31st December 2015. Patients with other forms of keratitis were excluded. We reviewed and extracted information from the case records. This included patient demographics, history, recorded risk factors, presenting visual acuity, treatment and outcome.

Data were analysed in STATA v14. The main study variables were presentation time, use of traditional eye medicine, use of "other eye medicine", history of trauma, presenting vision, follow-up rate, final visual acuity and loss of the eye. Visual acuity was categorised according to the WHO classification system[14]. Presentation time was classified as early (1-3 days) or late (4 days and above)[15]. For the purposes of this analysis we categorised poor presenting vision to be worse than 6/60[6]. Logistic regression analysis was used to identify factors associated with poor presenting vision.

RESULTS

Two hundred and seventy three patient records with clinically diagnosed bacterial or fungal keratitis were enrolled. Figure 1 shows the enrolment process.

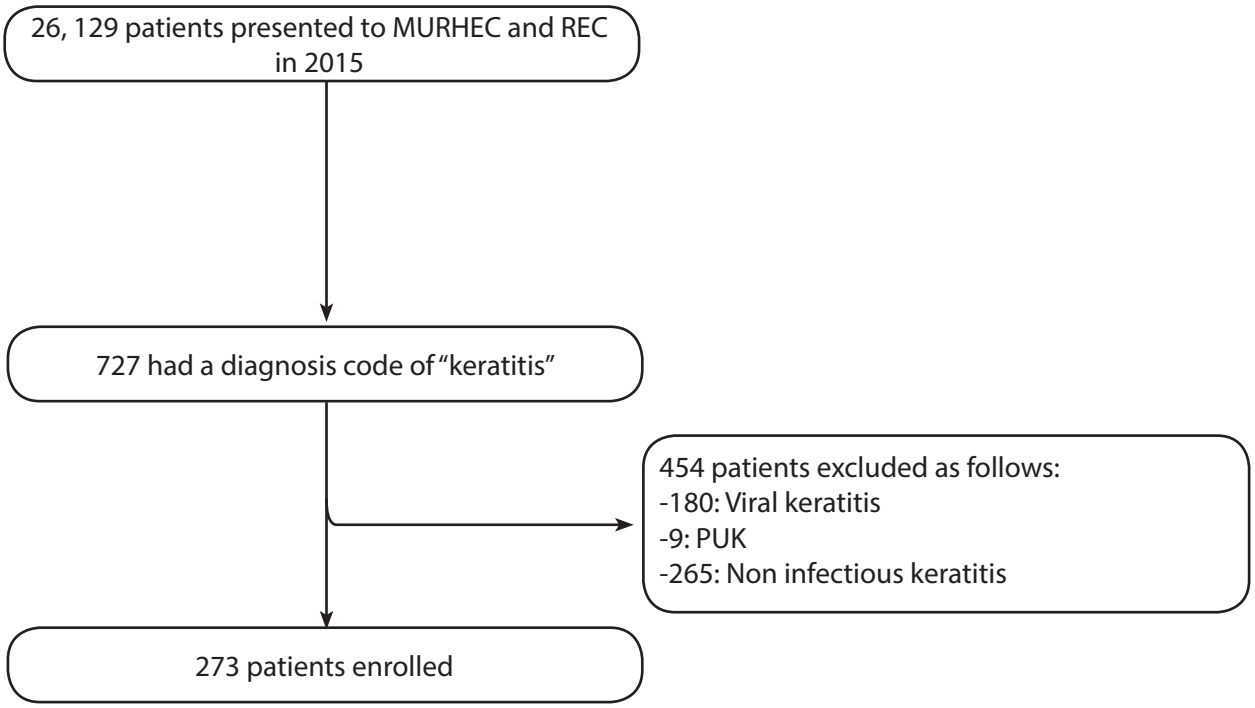

Figure 1: Patient chart evaluation for enrolment

Of the 273 individuals with bacterial or fungal keratitis, 178 (65%) were male (Table 1). Their median age was 36 years (IQR19–55 years, Total Range 1–104 years). The time between the onset of symptoms and presentation was skewed: median 7 days, IQR 0–21days, total range 0–366 days. Seventy three patients (30%) presented early (≤3 days) and 166 (70%) patients presented late (≥ 4 days). Patients had to travel considerable distances to reach the eye units: median 80km, IQR 45-99 km, total range 1-378km. There was no microbiology data recorded. At presentation, visual acuity was documented in 220 (81%) out of 273(81%) patients of which 80/220 (36%) had a vision worse than 6/60.

Table 1: Baseline characteristics of all 273 individuals with microbial keratitis

Variable	Median	IQR	(Total Range)
Age (years)	36	19-55	(1-104)
Distance from eye hospital (km)	80	45-99	(1-378)
Time to presentation (days)	7	0-21	(0-295)
Variable	N	Count	(%)
Sex	273		
• Male		178	(65%)
• Female		95	(35%)
Trauma*	88	59	(67%)
Prior treatment ŀ	154	147	(96%)
Traditional eye medicine use ǂ	162	69	(43%)
Hypopyon	271	42	(15%)
Visual acuity at presentation §	216		
6/5-6/18		107	(48%)
6/24-6/60		33	(15%)
5/60-3/60		8	(4%)
2/60-1/60		13	(6%)
0.5/60-PL		48	(22%)
NPL		11	(5%)

*Data not recorded in all clinical notes, denominator (N) indicates the number of records where reference to this variable was made. Out of the 273 patients, 88 had data on whether there was trauma or not (59/88, 67%, positive).

ŀ 147/154 (95%) patients reported prior use of some other eye medicine other than TEM, but the specific type was not recorded.

ǂ 162 patients had data on whether they had used Traditional Eye Medicine (TEM) or not (69/162, 43%, positive). The different types of traditional medicine were not recorded in the charts.

§ Only 216 out of 273 patients had recorded presenting vision.

PL = Perception of Light; NPL = No Perception of Light

Table 2: Logistic regression for factors associated with a poor presenting vision among patients with microbial keratitis

Variable	Univariate analysis			Multivariate analysis		
	Crude OR	(95% CI)	P-value	Adjusted OR	(95% CI)	P-value
Age	1.02	(1.01-1.03)	0.016			
Sex (being female)	1.19	(0.66-2.13)	0.564			
Distance (for every 1 Km increase)	1.02	(1.01-1.03)	0.001	1.02	(1.01-1.03)	0.002
TEM use	4.66	(2.18-9.95)	0.001	5.13	(2.17-12.1)	0.001
				5.19	(2.24-12.0)	0.001 ŀ
Trauma	1.28	(0.44-3.75)	0.645			
Delayed presentation	1.49	(0.75-2.92)	0.247			

In this model, there was a lot of missing data in the patient charts that not all the patients with reported baseline vision could be used for the analysis. The final model had 120 observations.

ŀ TEM adjusted for delayed presentation.

The factors associated with a poor presenting vision (<6/60) were analysed. The univariable and multivariable logistic regression models are presented in Table 2. Poor vision at presentation (<6/60) was associated with increasing distance from home to hospital (OR 1.02, 95% CI 1.01-1.03, p=0.002) and TEM use (OR 5.13, 95% CI 2.17-12.1, p=0.001).

DISCUSSION

This audit highlights factors associated with a poor presenting vision. Multiple factors were hypothesised to contribute to poor outcomes. These included large distances from the eye hospital, delayed presentation, trauma and Traditional Eye Medicine (TEM).

In this audit, almost half of the patients with recorded information on TEM reported having used TEM and this was strongly associated with worse presenting vision, even after controlling for delay in presentation. Many people probably choose to try TEM for several days before attending hospital as it can be easily obtained within or close to home. Its use appears to contribute to poor outcomes, substantially adding to the risk of poorer presenting vision. In Uganda, TEM is usually made from plant products. This is concerning, as such substances may be toxic or harbour infectious agents, such as fungal spores[16, 17].

A large distance to the eye hospital was strongly associated with poor presenting vision. The units included in this audit constitute the referral centres for the whole region and many of the patients came from substantial distances to seek treatment. While the evidence from our data was limited, distance is probably an important factor in the presentation, course and outcome of MK in our setting.

This retrospective audit had several limitations. Visual acuity was not recorded consistently for all patients at presentation and follow-up. Presenting vision was available in about 81% of the patients. From a clinical management point of view this is an important audit learning point. We have already introduced new procedures that ensure the consistent recording of vision data for all patients. It is possible that this might have introduced some systematic bias, with people with poorer vision being less likely to have this documented than those with better vision.

Loss to follow-up is generally a significant challenge in this region and makes it difficult to evaluate outcomes. Follow-up data was largely missing and so the analysis was based on presenting vision as a proxy of outcome[18].

During 2015, samples were not sent for microbiological investigations, therefore, diagnosis and treatment choices were based purely on clinical evaluation. In the absence of a microbiological diagnosis, diagnostic uncertainty remains high, likely resulting in failure to treat appropriately[19, 20]. Following this audit, we have started a routine ocular microbiology service for all patients with MK.

CONCLUSIONS

This audit reflects the factors associated with a poor presentation among patients with MK. Delayed presentation, traditional eye medicine use, lack of laboratory support are all factors which need to be addressed in the effort to reduce avoidable blindness. Good quality data collection and research into strategies to manage MK are clearly needed.

ACKNOWLEDGMENT

We would like to appreciate Mr Gilbert Arinda and Ms. Pauline Boonabaana for tirelessly digging out the charts of these patients. Dr John Onyango, Dr Freddy Mbumba and Mr Richard Owomugasho for giving us permission to access these files.

Funding: SA is supported by a Research Fellowship from the Commonwealth Eye Health Consortium, funded by The Queen Elizabeth Diamond Jubilee Trust. MJB is supported by the Wellcome Trust (098481/Z/12/Z and 207472/Z/17/Z). The funding organisations were not involved in the design, collection, analysis and review of this manuscript.

Consent for publication: Not applicable for this audit. All data were anonymized after extraction from clinical notes.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

REFERENCES

1. Bennett JE, Dolin R, Blaser MJ. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases E-Book: Elsevier Health Sciences; 2014.
2. Whitcher JP, Srinivasan M. Corneal ulceration in the developing world--a silent epidemic. *Br J Ophthalmol*. 1997; **81**(8):622-623.
3. Whitcher JP, Srinivasan M, Upadhyay MP. Corneal blindness: a global perspective. *Bull World Health Org*. 2001;**79**(3):214-221.
4. Titiyal JS, Negi S, Anand A, Tandon R, Sharma N, Vajpayee RB. Risk factors for perforation in microbial corneal ulcers in north India. *Br J Ophthalmol.* 2006; **90**(6):686-689.

5. Pharmakakis NM, Andrikopoulos GK, Papadopoulos GE, Petropoulos IK, Kolonitsiou FI, Koliopoulos JX. Does identification of the causal organism of corneal ulcers influence the outcome? *Eur J Ophthalmol.* 2003;**13**(1):11-17.
6. Burton MJ, Pithuwa J, Okello E, Afwamba I, Onyango JJ, Oates F, *et al*. Microbial keratitis in East Africa: why are the outcomes so poor? *Ophthalmic Epidemiol*. 2011; **18**(4):158-163.
7. Leck AK, Thomas PA, Hagan M, Kaliamurthy J, Ackuaku E, John M, *et al*. Aetiology of suppurative corneal ulcers in Ghana and south India, and epidemiology of fungal keratitis. *Br J Ophthalmol*. 2002; **86**(11):1211-15.
8. Mafwiri M, Kanyaro N, Padhan D, Sanyiwa A, Sangawe J, Kinabo N. The microbial aetiology of corneal ulceration among patients attending a tertiary referral centre in Dar es Salaam. *J Ophthalmol East Central Southern Africa*. 2013;**16**(1): 25-28.
9. Poole TR, Hunter DL, Maliwa EM, Ramsay AR. Aetiology of microbial keratitis in northern Tanzania. *Br J Ophthalmol*. 2002; **86**(8):941-942.
10. Carmichael TR, Wolpert M, Koornhof HJ. Corneal ulceration at an urban African hospital. *Br J Ophthalmol*. 1985; **69**(12):920-926.
11. Hagan M, Wright E, Newman M, Dolin P, Johnson G. Causes of suppurative keratitis in Ghana. *Br J Ophthalmol.* 1995; **79**(11):1024-28.
12. Wani MG, Mkangamwi NA, Guramatunhu S. Prevalence of causative organisms in corneal ulcers seen at Sekuru Kaguvi Eye Unit, Harare, Zimbabwe. *Central Afr J Med*. 2001; **47**(5):119-123
13. Oladigbolu K, Rafindadi A, Abah E, Samaila E. Corneal ulcers in a tertiary hospital in Northern Nigeria. *Annals Afr Med*. 2013;**12**(3):165.
14. Organization WH. Change the definition of blindness. Disponível no endereço eletrônico *http://www who int/blindness/ ChangetheDefinitionofBlindness pdf. 2008.*
15. Getshen K, Srinivasan M, Upadhyay MP, Priyadarsini B, Mahalaksmi R, Whitcher JP. Corneal ulceration in South East Asia. I: a model for the prevention of bacterial ulcers at the village level in rural Bhutan. *Br J Ophthalmol*. 2006; **90**(3):276-278.
16. Courtright P, Lewallen S, Kanjaloti S, Divala DJ. Traditional eye medicine use among patients with corneal disease in rural Malawi. *Br J Ophthalmol*. 1994; **78**(11):810-812.
17. Yorston D, Foster A. Traditional eye medicines and corneal ulceration in Tanzania. *J Trop Med Hygiene*. 1994; **97**(4):211-214.
18. Prajna NV, Krishnan T, Mascarenhas J, Srinivasan M, Oldenburg CE, Toutain-Kidd CM, *et al*. Predictors of outcome in fungal keratitis. *Eye* (Lond). 2012; **26**(9):1226-31.
19. Dalmon C, Porco TC, Lietman TM, Prajna NV, Prajna L, Das MR, *et al.* The clinical differentiation of bacterial and fungal keratitis: a photographic survey. *Invest Ophthalmol Visual Sci.* 2012; **53**(4):1787-91.
20. Leck A, Burton M. Distinguishing fungal and bacterial keratitis on clinical signs. *Comm Eye Health/Intern Centre for Eye Health*. 2015; **28**(89):6-7.