Original Article

Demographic and socioeconomic barriers and treatment seeking behaviors of patients with infectious keratitis requiring therapeutic penetrating keratoplasty

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Purpose: To understand demographic and socioeconomic barriers and treatment-seeking behaviors of patients with infectious keratitis requiring therapeutic penetrating keratoplasty (TPK) in a developing country. **Methods:** This prospective non-comparative questionnaire- based study included all patients presenting to Aravind Eye Hospital, Madurai with infectious keratitis that eventuated to TPK between November 2015 and October 2016. A structured questionnaire was administered on post-operative day 3 to collect data on the demographic details, predisposing factors, prior treatment received, and treatment expenditures. **Results:** In total, 227 patients underwent TPK between November 2015 and October 2016 for infectious keratitis. The majority of patients were males (n = 132, 58.1%), illiterate (n = 129, 56.8%), and had a family monthly income of less than INR 6000 (n = 142, 62.5%). Most of the patients (n = 163, 71.8%) had prior treatment with an ophthalmologist before presenting to our hospital. The mean distance travelled to reach our centre was 269.2 ± 298.5 km. The mean duration of disease before the presentation was 20.3 ± 21.1 days. Corneal smear was positive for fungus in 163 (88.1%) and *Aspergillus* was the most commonly isolated fungi in 55 (41.3%) cultures. The mean total cost of treatment was INR 8752.87 ± 7615.39 per patient. There was a positive correlation between the duration of the disease (rho 0.19, P = 0.0034) and the costs of treatment (rho 0.2, P = 0.0024) with the distance travelled by the patient. **Conclusion:** Patients who travelled a farther distance had a delayed onset of presentation and spent significantly more than their respective counterparts.

Access this article online

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_1821_18

Quick Response Code:

Key words: Demographic profile, Infectious keratitis, socioeconomic profile, therapeutic penetrating keratoplasty

Infectious keratitis disproportionately affects people of working age, which can cause a significant financial burden in terms of lost wages and medical expenses.[1,2] A significant proportion of these ulcers fail medical treatment and eventually require therapeutic penetrating keratoplasty (TPK).[3,4] Commonly reported risk factors for failure of medical therapy include large ulcer size, presence of hypopyon, and the virulence of the infecting organism.[5] Severe filamentous fungal corneal ulcers (particularly *Aspergillus spp*), which are more common in tropical climates, eventuate to TPK in up to 50% of cases.[6,7] Other factors such as delay in seeking treatment, high cost associated with the treatment, lack of access to appropriate care, and non-compliance to treatment regimen may all play a role in the failure of medical treatment in resource-poor settings.

While there have been studies which examine barriers to receiving care in other ophthalmologic conditions such as diabetic retinopathy, glaucoma, and cataracts, data regarding infectious ulcers are lacking.[8,9] A clear understanding of the economic and social factors that result in a delay in treatment and likely increase the likelihood of poor outcome is necessary so that appropriate strategies can be implemented to reduce barriers to care. Here, we evaluate the social and economic barriers to care and the treatment-seeking behaviors of the patients with infectious keratitis requiring TPK at one tertiary referral center in India.

Methods

We conducted a prospective non-comparative questionnaire-based study, including all patients presenting with infectious keratitis that eventuated to TPK between November 2015 and October 2016 at Aravind Eye Hospital (AEH), Madurai. The study protocol followed ethical guidelines on human subjects given by the Indian Council of Medical Research and was approved by the Institutional Review

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Manuscript received: 01.11.18; Revision accepted: 24.04.19

Cite this article as: Shah H, Radhakrishnan N, Ramsewak S, Chiu S, Joseph S, Rose-Nussbaumer J, *et al*. Demographic and socioeconomic barriers and treatment seeking behaviors of patients with infectious keratitis requiring therapeutic penetrating keratoplasty. Indian J Ophthalmol 2019;67:1593-8.

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All patients, regardless of their ability to pay, were examined by a corneal specialist and underwent scraping and corneal cultures per institutional protocol.[10] Every patient was prescribed appropriate treatment, as determined by the treating physician based on clinical diagnosis and microbiological studies.[10] The patients were advised to undergo TPK if they had a full thickness corneal perforation, were determined to have an impending perforation, had involvement near the corneal limbus, or progressed clinically despite appropriate medical therapy. The surgery was performed completely free of charges for patients in the non-paying section and patients on their own covered costs of transportation, food, and medicines. Patients in the paying section paid for the cost of the entire treatment course out of pocket. All patients underwent TPK following the standard surgical procedures in the dedicated cornea surgical room at the paying section of AEH.

Patients were interviewed by the respective operating surgeons on post-operative day 3 using a structured questionnaire translated to the patients' mother tongue (available as online only supplementary material). The questionnaire developed in consultation with a team of experts was pre-tested, modified, and validated after pilot testing, and included questions relating to patient demographics (part A), systemic illness history (part B), pre-AEH history ((part C), and history and management at AEH (part D). All the relevant clinical information were captured as secondary information from the patients' medical records. We used the modified version of Kuppusamy's socioeconomic scale to categorize the patients.[11] We collected various costs incurred by the patients (Section D) and calculated the total treatment cost for the patient.

STATA version 14.0 was used for all statistical analyses. Mann–Whitney U-test was used for categorical variables, and Kruskal–Wallis test was used for continuous variables. Spearman rank correlation was used to find the correlation between distance travelled and the duration of disease and the costs involved in the treatment. Conversion of low visual acuity like counting fingers and hand motions were based on previously reported protocols.[12]

Results

Demographic and socioeconomic factors

Out of the 2203 corneal ulcer patients examined in the study period, 227 patients underwent therapeutic keratoplasty. Table 1 outlines their demographic and socioeconomic status. In total, 132 (58.2%) patients were male and the mean age at presentation was 52.1 years (SD ± 14.7 years). The most common occupation was agricultural work (*N* = 99, 43.6%). More than half were illiterate (N = 129, 56.8%). In all, 86 (37.8%) patients were the primary provider for their family. Monthly family income was less than INR 3000 for 72 (31.7%), between INR 3001 and 6000 for 70 (30.8%), between INR 6001 and 10,000 in 37 (16.3%), and more than INR 10,000 in 48 (21.1%). The vast majority of patients were from a rural background 184 (81.4%), 36 (15.9%) were from a semi-urban background, and 6 (2.6%) were from an urban background. The mean distance travelled to AEH was 269.2 ± 298.5 km (Median 150 km, IQR 80–150 km). In all, 84 patients (37%) had to travel less than 100 km to come to the hospital, 88 (38.7%) had to travel between 101 and 300 km, 11 (4.8%) patients had to travel between 301 and 500 km, and 44 (19.3%) patients had travelled more than 500 km for treatment.

Table 1: Demographic details of patients who underwent TPK

Demographic details	*n*=227	Percentage
Gender		
Male	132	58.2
Female	95	41.8
Occupation		
Agriculture worker	99	43.6
Homemaker	30	13.2
Manual labourer	25	11
Farm landowner	12	5.2
Industrial worker	8	3.5
Student	6	2.6
Shop owner	2	0.8
Professional	2	0.8
Unemployed	13	5.7
Others	30	13.2
Education		
Illiterate	129	56.8
Primary level	58	25.5
Secondary level	33	14.5
College	7	3.1
Family Income per month (Rs)		
<3000	72	31.7
3001-6000	70	30.8
6001-10,000	37	16.3
10,001-20,000	31	13.6
>20,000	17	7.4
Breadwinner of the family		
Yes	86	37.89
No	141	62.11
Job regularity		
Regular	95	41.8
Seasonal	45	19.8
Irregular	38	16.7
None	49	21.5
Residence		
Rural	184	81.4
Semi-urban	37	16.2
Urban	6	2.6

Prior medical history

Of the 227 patients in the study, 30 (13.2%) had a history of diabetes mellitus. In total, 37 (16.2%) patients had undergone prior ophthalmic surgery. Of these patients, 27 (11.8%) patients had cataract surgery, 5 (2.2%) had corneal transplant, 2 (0.9%) had lacrimal sac surgery, 2 (0.89%) had lid surgery, and 1 (0.4%) had trabeculectomy. None of them had ophthalmic surgery in the recent past. One (0.4%) patient was on anti-glaucoma medications.

Of the 227 patients, 108 (47.5%) had a history of ocular trauma. Of the 108 patients who reported injury, vegetable matter was implicated in 45 (41.6%) individuals, sand or dust particles were reported in 34 (31.4%) individuals, and a history of injury by insects was elicited in 13 (12%) individuals. Of these individuals, 55 (50.9%) had trauma at a farm or their workplace, 39 (36.1%) had an injury at home, and 14 (12.9%) had an injury elsewhere. Of the 227 patients, 28 (12.3%) had self-medicated with either native medicines or medicines purchased over-the-counter.

Treatment prior to presentation

Of the 227 patients, 163 (71.8%) sought treatment by an ophthalmologist prior to presenting to AEH. Of these, 134 (82.2%) had visited 1 hospital, 25 (15.3%) had visited 2 hospitals, 3 (1.8%) had visited 3 hospitals, and 1 (0.6%) patient had visited 4 hospitals. Their treatment prior to presentation at AEH included antibiotics in 26 (15.9%), antifungals in 41 (25.1), and 20 (12.2%) received both antibacterial and antifungals. Two patients reported being treated with topical steroids (1.2%) and 74 (45.3%) did not have the details of the treatment they received. The nearest eye care provider was at an average distance of 19.7 km (SD ± 24.2 km) and was a private practitioner/hospital for 98 (43.1%) patients, a government primary or secondary health centre for 68 (29.9%) patients and a part of the AEH healthcare system (primary vision centre) for 29 (12.7%) patients. In total, 32 (14.1%) patients were not aware of their nearest eye care provider. The mean direct cost of treatment (without taking into account the travel costs or lost wages) for a patient before coming to AEH was INR 1829.11 ± 2789.05.

Treatment in AEH

The mean duration of symptoms prior to coming to AEH was 20.3 ± 21.1 days (Median 14 days, Interquartile range IQR 7–22.5) [Table 2]. The mean logMAR visual acuity at presentation was 2.3 (SD ± 0.7). Reasons for patients to come to AEH for treatment included being advised by a friend/relative in 76 (33.4%) patients, referred by previous facility in 73 (32.1%) patients, no perceived improvement with previous treatment in 31 (13.6%) patients, easy accessibility in 9 (3.9%) patients, cultural belief in 4 (1.7%) patients, and no particular reason in 34 (14.9%). Of the 227 patients, 126 (55.5%) were treated in the paying section, 101 (44.4%) in the non-paying section, 218 (96%) patients had at least 1 accompanying person, and none in 9 (3.9%). Of these 218 patients, 193 (88.5%) had brought one accompanying person, 24 (11%) had 2 accompanying persons, and 1 (0.4%) patient had 3 accompanying persons.

Of the 227 patients seen at AEH, 71 (31.2%) patients were advised to have therapeutic keratoplasty during their first consultation at AEH, whereas 156 (68.7%) received medical treatment in AEH before they eventually required therapeutic keratoplasty. Of these 156 patients, 34 (21.7%) patients had 1 visit at AEH, before TPK was advised, 30 (19.2%) had two visits, 50 (32%) had three visits, 29 (18.5%) had four visits, and 13 (8.3%) had 5 or more visits to AEH before TPK was advised. This gives a mean average of 2.7 visits per patient at AEH, before undergoing TPK. The average duration of treatment for these 156 patients before TPK in AEH was 21.3 (±23.7) days. Corneal smear positivity was seen in 185 (81.4%) patients and negative in 42 (18.5%) [Table 3]. Of these 185 patients, 163 (88.1%) were positive for fungus and 22 (11.8%) were positive for bacteria. Culture was positive in 150 (66%) patients and no growth of organism was seen in 77 (33.92%) patients. Of the 150 culture positive patients, 133 (88.6%) were positive for fungus, 15 (10%) patients were positive for bacteria, and 2 (1.3%) were positive for *Acanthamoeba spp*. The most common fungi isolated in culture was *Aspergillus spp* in 55 (41.3%) patients followed by *Fusarium spp* in 52 (39%). The most common bacteria isolated in culture was *Pseudomonas spp* in 7 (46.6%) patients followed by *Streptococcus pneumoniae* in 2 (13.3%) patients. Of the 71 patients who underwent TPK in their first visit of AEH, 7 (9.8%) were smear positive for bacteria, 44 (61.9%) were smear positive for fungi, and smear negative in 20 (28.1%) patients. Whereas of the 156 patients who received medical therapy before undergoing therapeutic keratoplasty, 15 (9.6%) were smear positive for bacteria,

Table 2: Management at our centre of patients who underwent TPK

Parameters	*n*=227	Percentage
Distance travelled (km)		
≤100	84	37
101-300	88	38.7
301-500	11	4.8
>500	44	19.3
Reasons for coming to AEH		
Advised by friend	76	33.4
Referred by previous doctor	73	32.1
No improvement with prior treatment	31	13.6
Cultural belief	4	1.7
Easy access	9	3.9
No particular reason	34	14.9
Stream of admission		
Paying	126	55.5
Non-paying	101	44.4
Accompanying person		
0	9	3.9
1	193	88.5
2	24	11
3	1	0.4
Medical treatment before surgery		
Yes	156	68.7
No	71	31.2
Number of medical treatment visits before surgery		
1	34	21.79
2	30	19.23
3	50	32.05
4	29	18.59
>4	13	8.33
Indications for TPK[a]		
Perforation	119	52.42
Impending perforation	18	7.93
Threatening limbal involvement	41	18.06
Progression with maximum medical therapy	105	46.26

[a]Many patients had more than one indication for TPK

119 (76.2%) were positive for fungi, and 22 (14.1%) were smear negative.

The indications for TPK were corneal perforation in 119 (52.4%) patients, impending perforation in 18 (7.9%) patients, limbal involvement in 41 (18%), and progression despite treatment in 105 (46.2%). The average expenditure for the patient before TPK was INR 8752.87 ± 7615.39. This included the travel expenditure (INR1446.21 ± 2737.26), treatment expenditure (INR 3649.52 ± 4832.69), lost wages (INR 2265.97 ± 3570.44), and expenditure by the accompanying person (INR 1840.21 ± 2943.97).

There was no difference in the duration of the disease across gender (*p* 0.161), financial status (*p* 0.722), and literacy levels (*p* 0.355). The breadwinners (*p 0.02*), the higher income groups (*p 0.0001*), and those with higher levels of education (*p 0.0001*) reported to have spent significantly more money for treatment [Table 4]. Patients who had to travel longer distances to reach AEH were found to have a more delayed presentation (*rho 0.19, P 0.0034*) and had spent more money on treatment (*rho 0.2, P 0.0024*) compared to those who traveled shorter distances.

Discussion

Corneal ulcers have a distinct and unique presentation compared to other common ophthalmologic conditions including cataracts, diabetic retinopathy, and glaucoma. While the latter group of conditions are gradual in onset over months to years and may be asymptomatic, corneal ulcers develop acutely and are incredibly painful. Therefore, the patients should be expected to have increased awareness of their clinical condition and actively seek treatment for this condition. At the same time, the urgent acute nature of the condition might not have allowed them to plan treatment strategies. Some patients decided to self-medicate with alternative remedies, which may have led to additional delays in receiving appropriate treatment. Nevertheless, these delays can potentially cause worse outcomes, given progression of infectious corneal ulcers leading to perforation and surgical management. There needs to be more education regarding signs and symptoms of corneal ulcers and emphasis on their sight-threatening complications if left untreated. Studies have shown that microbial keratitis after corneal abrasion can be prevented at the village level by simple public health strategies using antibiotic and antifungal prophylaxis tailored to the prevalence of pathogens causing corneal ulcers in the population.[13-16]

Table 3: Smear and culture results of patients with infectious keratitis requiring therapeutic keratoplasty

Microbiological Profile	Number (%)
Total number of patients	227
Smear positive	185 (81.4%)
Bacteria	22 (11.8%)
Fungus	163 (88.1%)
Smear negative	42 (18.5%)
Culture positive	150 (66%)
Bacteria	15 (10%)
Fungus	133 (88.6%)
Acanthamoeba	2 (1.3%)

A large portion of patients (163, 71.8%) received ophthalmological care prior coming to AEH and the average distance travelled to receive that care was 20 km. Anecdotally, it is well known that most treatment planning at remote primary and secondary care locations are based on presumptive clinical diagnosis and not necessarily by a microbiological confirmation. An increase in the awareness of the regional variation of the risk factors and the aetiological agents for infectious keratitis will help in early diagnosis. A basic microbiological examination using smears should be encouraged at these sites, especially in a setting where bacteria and fungi can cause infections in almost equal proportions. It is also well known that it is difficult to differentiate between bacterial and fungal keratitis in all cases and microbiological investigations are essential to confirm the diagnosis.[17] Hence, development of preferred practice patterns for treatment of corneal ulcers will help in prompt treatment of patients by local ophthalmologists and can reduce associated visual disability.

Even amongst patients attending AEH, it is also important to understand that a significant proportion of patients with this condition (70%) were not advised primary TPK. These patients eventually required a TPK, after making multiple visits to AEH. This underscores the importance of the difficulty in decision making for subjecting a patient to undergo TPK even in a tertiary care setting. Fungal culture and genus identification takes a longer time than bacterial culture and hence organism directed therapy is difficult. In a tertiary care set up like AEH, the patients are not necessarily seen by the same consultants at every follow-up and hence a photographic documentation and a standardized measurement of the ulcers at each visit may be important. The indications for advising surgery may also need to be standardized even further. Perforation was the most common indication for therapeutic keratoplasty, and it is well known that the outcomes of TPK for perforated corneal ulcers are worse than that of TPK for non-perforated ulcers.[18] Delay in access to appropriate medical treatment, virulence of the causative organism, increased resistance, and non-compliance due to long costs and duration of treatment are thought to be the reasons for treatment failure.

Patients treated in the free section of AEH are still required to pay for their medications, which creates an economic barrier. In addition, 90% of the patients required an accompanying person with them to escort them to the hospital. These costs of travel and the lost wages of the accompanying person may also play a major role in the treatment-seeking behaviour of patients with painful debilitating corneal ulcers. Previous studies looking at glaucoma medication use in the AEH population have shown similar issues with adherence and compliance.[8,9] Unfortunately, poor compliance causes serious and rapid visual morbidity in corneal ulceration and hence strategies should be developed to ensure that the patient actually is compliant with the prescribed treatment.

This study demonstrates that removing barriers to care, whether they may be economic, social, or otherwise and bringing the healthcare system closer to the patient can potentially improve visual outcomes. For example, AEH has established a growing number of vision centres in the communities of south India. These vision centres, staffed by trained ophthalmic technicians, provide basic vision care in smaller rural communities with the help of tele-ophthalmology.

Table 4: Comparison of demographic details with a duration of disease before presentation to our centre and the total costs of treatment

Parameters	Duration (in days)			Costs of Treatment (Rs)	
	n	Median (IQR)	*P*	Median (IQR)	*P*
Gender			0.161*		0.09*
Male	132	15 (7-25)		7250 (3200-12,650)	
Female	95	10 (5-20)		5240 (3250-9840)	
Breadwinner			0.141*		0.03*
Yes	86	15 (7-30)		7750 (3750-13,310)	
No	141	12 (6-20)		5700 (3000-10,700)	
Income (Rs)			0.722+		0.0001+
<3000	72	10 (5-26)		4350 (2400-7800)	
3000-6000	70	15 (7-20)		6050 (3000-11,750)	
6000-10,000	37	15 (7-25)		7500 (3700-10,600)	
10,000-20,000	31	14 (7-25)		11,700 (7600-16,400)	
>20,000	17	12 (7-15)		15,000 (4700-25,040)	
Education			0.355+		0.0001+
Primary	58	12 (7-30)		8200 (4000-14,800)	
Secondary	33	15 (7-25)		12,100 (7500-16,000)	
College	7	20 (8-60)		20,130 (13,700-28,000)	
Illiterate	129	14 (7-20)		5200 (2700-8000)	

*Mann-Whitney U-test +Kruskal-Wallis test

Patients presenting there with corneal ulcers are started on antimicrobials and urgently referred to AEH for further treatment. It is likely that early and appropriate treatment at points of primary care reduces the delay of treatment and ocular morbidity thus reducing the incidence of TPK.

There are a few limitations to this study. One issue is that the data were survey based, so it is not possible to verify the accuracy of the data collected from patients. Another limitation of this study was that the data of the patients whose corneal ulcer healed with medical therapy were not captured.

Conclusion

In summary, this study captures the demographic data of patients diagnosed with infectious keratitis requiring therapeutic keratoplasty from the beginning of the symptoms until TPK. Health education to encourage use of safety eyewear, awareness of the local ophthalmologists with regard to the epidemiology of the micro-organisms in the region, access to basic microbiological support at the primary care level, prompt referral, and the development of a preferred practice pattern may all play a role in preventing poor visual results following corneal ulceration.

Acknowledgements

The authors indicate no funding support. The authors indicate no financial conflict of interest in the design and conduct of the study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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