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Risk Factors Predicting Loss to Follow-up, Medication Noncompliance, and Poor Visual Outcomes Among Patients with Infectious Keratitis at a Public County Hospital

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Abstract

Purpose: Infectious keratitis is a vision-threatening condition requiring close follow-up and disciplined eye drop administration to achieve resolution. Although patients presenting to county hospitals often have more severe presentations, there is a paucity of risk and outcomes data in this setting. This study investigates risk factors predicting loss to follow-up (LTFU), medication noncompliance, and poor outcomes for infectious keratitis in the county hospital setting.

Methods: This was a retrospective case-control study at Zuckerberg San Francisco General Hospital and Trauma Center. Inclusion criteria were patients who had corneal cultures for suspected infectious bacterial or fungal keratitis between 2010–2021. Exclusion criteria were patients with viral keratitis only. Multivariable logistic regression was used to analyze the relationship of social and medical risk factors with LTFU, medication noncompliance, worsened visual acuity (VA), and delayed resolution time.

Results: Of 174 patients with infectious keratitis in this analysis, 69 (40.0%) had LTFU. Unemployment was associated with increased risk of LTFU (OR 2.58, $p = 0.049$) and worse final VA ($p = 0.001$). Noncompliance trended toward an association with homelessness (OR 3.48, $p = 0.095$). Increasing age correlated with longer resolution time, with each one-year increase associated with delayed resolution by 0.549 days ($p = 0.042$).

Conclusion: Patients experiencing unemployment, homelessness, or increased age demonstrate higher risk for treatment barriers including loss to follow-up and medication noncompliance, resulting in worse visual acuity and delayed time to resolution. These risk factors should be considered when determining the need for more deliberate follow-up measures in patients with infectious keratitis.

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Conflicts of Interest:

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Keywords

infectious keratitis; county hospital; loss to follow-up; social determinants; homeless

Introduction

Infectious keratitis requires close follow-up and frequent, disciplined eye drop administration in order to achieve resolution of the ulcer, preserve globe integrity, and prevent vision loss.[1] Patients presenting with infectious keratitis to county hospitals often demonstrate greater disease burden compared to those at private university hospitals[2] and are further encumbered by social determinants of health that hinder the successful management of corneal ulcers. Public county hospitals preferentially admit a high volume of patients with low or no insurance,[3] which in turn potentiates loss to follow-up (LTFU) and medication noncompliance. Analysis of overall ophthalmic presentations to an academic center emergency department showed that patients are at greater risk for LTFU if uninsured or on Medicaid coverage.[4] Meanwhile, lack of insurance coverage may pose financial barriers to medication compliance.[5]

Currently, there are no studies specifically focused on the association of social risk factors on infectious keratitis outcomes within the county hospital setting. Thus, there is an important need to better understand what variables can predict treatment course and outcomes of corneal ulcers within this vulnerable patient population. This study analyzes social risk factors predicting LTFU, medication noncompliance, and poor visual outcomes for patients with infectious keratitis in the public county hospital setting.

Materials and Methods

This retrospective study included all patients who received a corneal culture for suspected bacterial or fungal infectious keratitis between 2010 and 2021 at the Zuckerberg San Francisco General Hospital and Trauma Center (ZSFGH), in both the inpatient and outpatient settings. Exclusion criteria were patients with non-infectious or viral keratitis without suspected bacterial or fungal keratitis. This study was approved by the Institutional Review Board of the University of California, San Francisco (protocol number 19–28768) and conforms to the tenets of the Declaration of Helsinki.

Data for analysis were deidentified and collected via retrospective chart review within the hospital electronic medical record system. Collected data included demographic information (age, preferred gender (included trans individuals), race/ethnicity, preferred language, employment status, and housing status), medical and psychiatric comorbidities (including histories of substance abuse, psychiatric diagnoses, history of prior corneal ulcerations or abrasions, and contact lens use), and clinical data (symptom time prior to presentation at ZSFGH, initial best-corrected Snellen visual acuity (BCVA), and initial size of the ulcer). Snellen BCVA was converted to a logMAR estimate of Snellen = $\log_{10}\left(\frac{Snellen\ denominator}{Snellen\ numerator}\right)$.

Outcome metrics were defined as follows: time to ulcer resolution – days between initial presentation and closure of the epithelial defect; loss to follow-up (LTFU) – being out of care for at least 1 month with an active epithelial defect; final BCVA – as measured on the visit that the epithelial defect was first noted to be healed, or on the final visit if patient was lost to follow-up before the defect had healed; and medication noncompliance during the timeframe an epithelial defect was present. For patients that were classified as LTFU, medication compliance was assessed during the period that they were still following-up with the clinic.

Statistical analyses were performed using Stata Software (version 16.0). Chi-squared analysis was used to find associations between LTFU status and the various demographic and other risk factors. Logistic regression was used to find predictors of LTFU outcome and medication noncompliance. Linear regression was used to find predictors associated with worse final logMAR BCVA and longer corneal healing ulcer time. Patients for whom the information for specific variables was unknown due missing or ineligible notes were excluded from corresponding analyses. A p-value less than 0.05 was considered statistically significant.

Results

Demographics and Risk Factors for Loss to Follow-Up

A total of 174 patients with infectious keratitis were included in this study. Of those, 69 (39.7%) were considered non-loss to follow-up (non-LTFU) and 69 (39.7%) were considered LTFU, as defined above. The remaining 36 (20.7%) patients had unknown follow-up status and were not included in analyses involving LTFU. Of the LTFU patients, 5 patients had gaps in their care of at least one month but later followed-up.

Table 1 summarizes demographics and risk factors based on LTFU status. The non-LTFU group had a mean age of 47.3 years, while the LTFU group had a mean age of 46.0 years. Approximately 2/3 of patients were men, with a diverse ethnic distribution. There were no significant differences found in these demographic variables between the two groups.

Several factors showed significant associations with either non-LTFU or LTFU status on Chi-squared analysis. A listed non-English primary language was protective against LTFU, with non-English speakers consisting of 22 (31.9%) of non-LTFU, but only 6 (8.7%) of LTFU ($p = 0.016$). Patients in the non-LTFU group were more likely to be housed ($p = 0.017$), with 56 (81.2%) housed, 10 (14.5%) homeless, and 3 (4.3%) of unknown housing status. Patients in the LTFU group had a higher proportion of homeless individuals compared to non-LTFU ($p = 0.019$); 40 (58.0%) were housed, 28 (40.6%) were homeless, and 1 (1.4%) had unknown housing. Patients with LTFU showed increased risk for unemployment compared to non-LTFU, with 31 (44.9%) versus 16 (23.2%) unemployed ($p = 0.032$).

There was a trend toward an association between recreational drug use and LTFU, with 42 (60.9%) of patients reporting drug use compared to 26 (37.7%) of the non-LTFU group ($p = 0.058$). Ten (14.5%) of the non-LTFU group and 21 (30.4%) of the LTFU group had

a diagnosed psychiatric history ($p = 0.112$). Contact lens use and prior corneal abrasions and/or ulcers were not significantly associated with increased risk for LTFU.

Multivariable logistic regression was used to assess risk factors as predictors of the likelihood for LTFU (Table 2). The only significant predictor of LTFU was unemployment, with an odds ratio (OR) of 2.584 (95% CI: 1.003, 6.658; $p = 0.049$). Age, non-English language preference, homelessness, recreational drug use, and psychiatric history were not found to be significant predictors of LTFU.

Association of Loss to Follow-up Status on Presentation and Treatment Outcomes

Presenting clinical factors and treatment outcomes were analyzed based on follow-up status (Figure 1). LTFU had an average initial logMAR BCVA of 1.33 compared to 1.17 in non-LTFU ($p = 0.351$), and an average initial epithelial defect size of 8.53 mm^2 compared to 6.33 mm^2 in non-LTFU patients ($p = 0.304$). The average final logMAR BCVA improved to 1.13 for LTFU and 0.92 for Non-LTFU, and there was no statistically significant difference between the two groups ($p = 0.204$). Patients with LTFU had an OR of 2.670 for medication noncompliance, with 24 (51.1%) patients demonstrating noncompliance compared to 20 (29.0%) patients in the non-LTFU group ($p = 0.013$).

Logistic regression of potential risk factors for medication noncompliance (Table 3) revealed no significant associations. However, there was a trend toward an association between homelessness and medication noncompliance, with an OR of 3.478 (95% CI: 0.807, 15.000; $p = 0.095$). Recreational drug use, psychiatric history, unemployment, age, and non-English language preference were not significant predictors of medication noncompliance.

Association of Social Determinants on Treatment Outcomes

Demographic and social risk factors were assessed using linear regression for their likelihood of predicting worse final BCVA after corneal ulcer treatment (Table 4). Unemployment was the only significant predictor of worse final BCVA, with a coefficient of 0.690 (95% CI: 0.287–1.093, $p = 0.001$), translating to a 0.69 increase in logMAR visual acuity score if the patient was unemployed. Age trended toward an association, with a coefficient of 0.013 (95% CI: 0–0.027; $p = 0.066$). Race/ethnicity, non-English language preference, homelessness, recreational drug use, and psychiatric history were not significant predictors of worse final visual acuity.

Similarly, potential risk factors were assessed for their associations with a longer corneal ulcer healing time in a linear regression analysis (Table 5). Older age was significantly associated with delayed resolution, with a coefficient of 0.549 (95% CI: 0.022, 1.067; $p = 0.042$), representing an increase in clearance time by 0.549 days with each one-year increase in age. Non-English language preference, homelessness, recreational drug use, and psychiatric history were not found to be significantly associated with increased ulcer resolution time.

Discussion

In this study of patients presenting with infectious keratitis to a public county hospital, several important risk factors were identified for LTFU, medication noncompliance, and poorer visual outcomes. Significant risk factors for LTFU included homelessness, English as a primary language, and unemployment. Medication noncompliance was also significantly associated with LTFU and trended toward an association with homelessness. Worse final BCVA was seen in unemployed patients, and longer corneal ulcer resolution time was seen with increased age.

The outcome that differed most significantly between non-LTFU and LTFU patients was medication noncompliance, with over half of LTFU patients demonstrating noncompliance. Treatment for corneal ulcers often requires hourly administration of antibiotic drops, as well as multiple concurrent medications, making medication adherence a challenge for any patient.[1] This study emphasizes that loss to follow-up is associated with high risk for medication noncompliance.

The most significant risk factor for both LTFU and worse final BCVA was unemployment. Studies have shown that visual impairment is associated with unemployment[6,7] and that unemployment may be an independent risk factor for visual impairment.[8] Unemployment also increases the risk for delays to receiving health care and lower health care access.[9] The worse visual acuity associated with unemployment is likely related to healthcare access and medical insurance coverage. In the United States, medical insurance coverage is typically employer-based for the working age population, which represents the majority of our study population. It has been shown that the lack of medical insurance was the strongest predictor of working-class adults delaying necessary care.[10] Thus, our unemployed patients may have delayed seeking treatment or had concerns about follow-up costs which negatively impacted their clinical outcomes. Therefore, unemployed individuals may represent an especially vulnerable patient population that requires special attention to follow-up for comprehensive treatment of vision-threatening conditions such as infectious keratitis.

Longer corneal ulcer healing time was associated with increased age, with the time to clearance of the epithelial defect lengthening with each additional year of age. Age-related changes are known to occur within the cornea and ocular surface, including a loss of sensation and decreased function of meibomian and lacrimal glands.[11] Additionally, systemic immunity may diminish with age, allowing for increased prevalence and severity of infectious diseases.[12] These factors could help explain this study's finding of longer corneal ulcer healing time in aging patients, and may help guide expectations for needed length of treatment and follow-up for older patients presenting with infectious keratitis.

The results of this study concur with prior studies investigating risk for LTFU in patients who are homeless or recreational drug users. Having poor housing conditions has been associated with worse adherence to follow-up of other ophthalmic conditions, such as diabetic retinopathy.[13] In a systematic review of case reports on corneal complications due to crack cocaine use, 23% of all cases were lost to follow-up.[14] A significant proportion of

this study cohort (almost 40%) were recreational drug users, which may reflect an increased risk of LFTU.

Interestingly, the non-LTFU group had a higher percentage of non-English speaking patients, with 31.9% compared to just 8.7% of the LTFU group. This differs from the results of one study that examined predictors of loss to follow-up among patients being treated for proliferative diabetic retinopathy, which showed that having a non-English language as the primary language was positively associated with LTFU.[15] One study examining follow-up rates after presentation to the emergency department for ophthalmic conditions showed that the absence of an interpreter significantly increased the odds of LTFU among non-English speakers.[4] Another study looked at compliance with follow-up visits after emergency department visits overall, which showed that English speakers, non-English speakers who used an interpreter, and non-English speakers without interpreters all had similar rates of compliance with follow-up appointments.[16] It is unclear in this study analysis what the rate of interpreter use was for non-English speakers during visits with ophthalmic providers at ZSFGH. This may be a confounding variable for the rates of LTFU in English speakers compared to non-English speakers. Additional confounding variables in this study may be drug use, homelessness, and unemployment status, as English speakers had higher proportions of drug use (59.4%), homelessness (33.6%), and unemployment (52.4%) compared to non-English speakers (18.5%, 7.4%, and 16.0% respectively).

Limitations of this study include incomplete medical records for some patients, as there was a transition from paper to electronic medical record during the study period. The patient cohort was initially selected from lab data that was readily available in the medical record system, whereas not all ophthalmology clinic notes were transferred successfully. It was difficult to ascertain the true follow-up status for patients who did not have any eligible ophthalmology notes or who had only one note with no available records of clinic staff follow-up attempts, and they were thus excluded from the LTFU portion of this study. Within each analysis, a portion of patients were excluded due to incomplete medical records – 36 had unknown LTFU status, 55 had unknown medication compliance, 24 had unknown final BCVA, and 91 had unknown corneal ulcer healing time. This therefore limited the number of patient records that could be included within each specific analysis. Additionally, this study is confined to retrospective review at one public county hospital in an urban setting, and thus the results may not be widely applicable to all types of healthcare systems or patient populations.

In conclusion, this retrospective cohort study examined patients presenting with corneal ulcers to a public county hospital setting to find associations for loss to follow-up, medication noncompliance, and worse visual outcomes. The results suggest that patients experiencing unemployment, homelessness, and older age should receive particular attention and close follow-up for adequate treatment of infectious keratitis, as these individuals may be at risk for worse overall outcomes.

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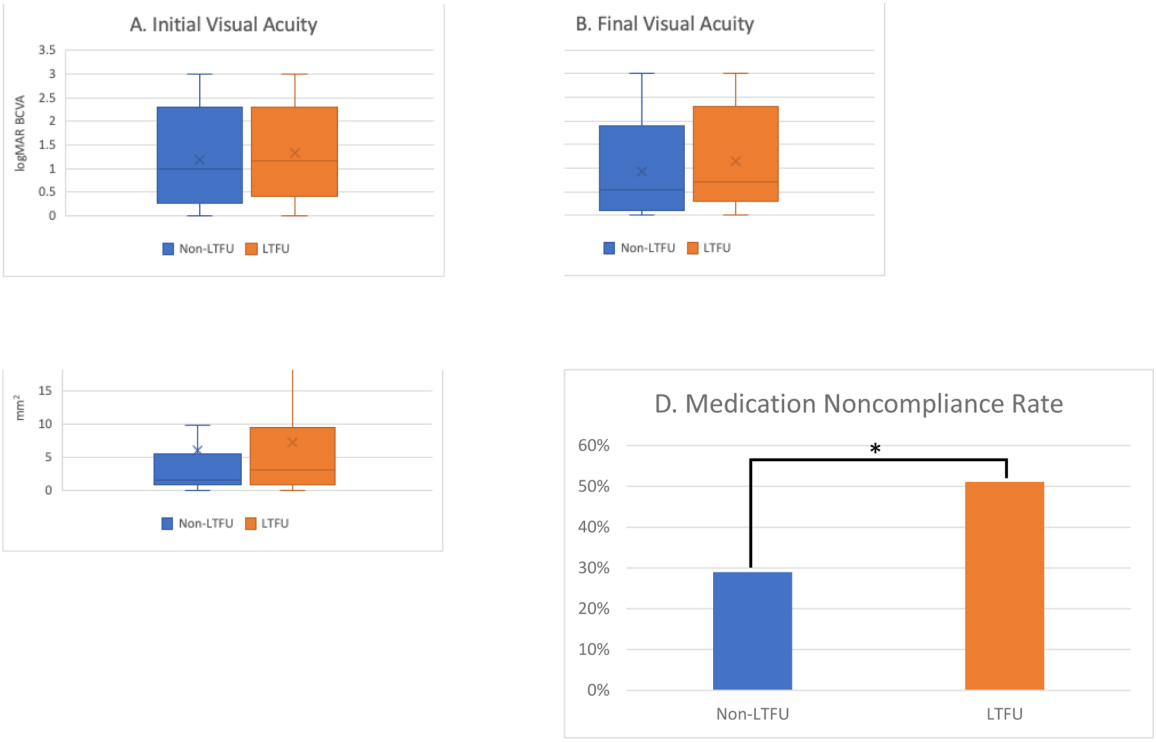

Figure 1:

Box and whisker plot of outcome variables – Initial and Final Best Corrected Visual Acuity (BCVA) and Initial Epithelial Defect Size, showing median value line and upper and lower quartiles, with errors bars as minimum and maximum values and x as mean marker. BCVA was measured in logMAR estimate of Snellen = $\log_{10}\left(\frac{Snellen\ denominator}{Snellen\ numerator}\right)$, with higher logMAR indicating worse BCVA.

Table 1.

Comparison of Demographics and Risk Factors Between Non-Loss to Follow-up and Loss To Follow-Up Patients

	Non-LTFU (n=69)	LTFU (n=69)
Age (years)		
Mean ± SD	47.3 ± 15.5	46.0 ± 12.1
Median (min-max)	46 (14–83)	48 (20–70)
Gender		
Man	43 (62.3%)	47 (68.1%)
Woman	26 (37.7%)	22 (31.9%)
Race/Ethnicity		
Native American	0 (0%)	0 (0%)
Asian / Pacific Islander	12 (17.4%)	10 (14.5%)
Black / African American	7 (10.1%)	12 (17.4%)
Hispanic / Latino(a)	19 (27.5%)	9 (13.0%)
White	15 (21.7%)	24 (34.8%)
Other	17 (24.6%)	14 (20.3%)
Housing Status *		
Housed	56 (81.2%)	40 (58.0%)
Homeless	10 (14.5%)	28 (40.6%)
Unknown	3 (4.3%)	1 (1.4%)
Employment Status *		
Employed / Retired	38 (55.1%)	22 (31.9%)
Unemployed / Disabled	16 (23.2%)	31 (44.9%)
Unknown	15 (21.7%)	16 (23.2%)
Non-English Preferred Language *	22 (31.9%)	6 (8.7%)
Recreational Drug Use	26 (37.7%)	42 (60.9%)
Contact Lens Use	22 (31.8%)	24 (34.8%)
Prior Corneal Abrasion or Ulcer	15 (21.7%)	17 (24.6%)
Psychiatric History	10 (14.5%)	21 (30.4%)

* $p < 0.05$ on Chi-squared analysis

LTFU = Loss to Follow-up, defined as being out of care for at least 1 month with an epithelial defect

Table 2.

Risk Factors Predicting Likelihood of Loss to Follow-Up

	Odds Ratio	95% Confidence Interval	*p*-value	% (n/N)
Age	0.985	(0.952, 1.020)	0.406	
Non-English Preferred Language	0.413	(0.101, 1.694)	0.220	8.7% (6/69)
Homelessness	1.647	(0.514, 5.280)	0.401	41.1% (28/68)
Recreational Drug Use	1.047	(0.381, 2.879)	0.929	62.7% (42/67)
Psychiatric History	1.101	(0.377, 3.214)	0.861	30.4% (21/69)
Unemployment	2.584 *	(1.003, 6.658)	0.049	58.5% (31/53)

* $p < 0.05$ on logistic regression analysis

A total of 69 patients were lost to follow-up (LTFU). %: the percentage of patients in the LTFU group with a positive risk factor. n: the number of patients in the LTFU group with a positive risk factor. N: the total number of patients in the LTFU group where information regarding the risk factor was available.

Table 3.

Risk Factors Predicting Medication Noncompliance

	Odds Ratio	95% Confidence Interval	*p*-value	% (n/N)
Age	1.016	(0.978, 1.055)	0.416	
Non-English Preferred Language	0.94	(0.167, 5.275)	0.944	15.2% (7/46)
Homelessness	3.478	(0.807, 15.0)	0.095	32.6% (15/46)
Recreational Drug Use	0.54	(0.145, 2.012)	0.359	56.5% (26/46)
Psychiatric History	1.90	(0.482, 7.412)	0.362	23.9% (11/46)
Unemployment	1.517	(0.467, 4.923)	0.488	51.3% (20/39)

* $p < 0.05$ on logistic regression analysis

Out of 119 patients analyzed for medication noncompliance, a total of 46 patients were documented to have medication noncompliance. %: the percentage of noncompliant patients with positive risk factor. n: the number of patients with a positive risk factor. N: the total number of noncompliant patients where information regarding the risk factor was available.

Table 4.

Risk Factors Predicting Worse Final Visual Acuity

	Coefficient	95% Confidence Interval	*p*-value
Age	0.013	(0, 0.027)	0.066
Non-English Preferred Language	0.35	(−0.242, 0.941)	0.244
Homelessness	−0.087	(−0.559, 0.385)	0.716
Recreational Drug Use	0.199	(−0.221, 0.620)	0.349
Psychiatric History	0.238	(−0.210, 0.687)	0.294
Unemployment	0.690 ***	(0.287, 1.093)	0.001

*** $p \leq 0.001$ on linear regression analysis

Table 5.

Risk Factors Predicting Longer Corneal Ulcer Healing Time

	Coefficient	95% Confidence Interval	*p*-value
Age	0.549 *	(0.020, 1.078)	0.042
Non-English Preferred Language	4.436	(−17.727, 26.599)	0.690
Unemployment	−2.24	(−20.173, 15.693)	0.803
Homelessness	16.823	(−6.312, 39.960)	0.151
Recreational Drug Use	10.358	(−8.032, 28.748)	0.264
Psychiatric Conditions	−17.114	(−38.244, 4.016)	0.110

* $p < 0.05$ on linear regression analysis