Anterior Segment Optical Coherence Tomography as a Follow Up Tool in Infectious Keratitis

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Abstract

Background: Infectious keratitis, a severe corneal condition, requires early empiric therapy due to a 48-hour diagnosis delay that can worsen outcomes. Anterior segment optical coherence tomography (AS-OCT) improves management by offering detailed scans of inflammation depth, stromal infiltration, and corneal thickness, enhancing diagnosis and treatment.

Objectives: To detect changes of AS-OCT in following up and prognosis of infectious keratitis.

Patients and methods: This study at Qena University Hospital involved 30 patients with infectious keratitis. Excluding those with retinal, corneal, or optic nerve diseases, patients were assessed on presentation and at 7, 14, 28 days, and 6 weeks using AS-OCT for corneal and infiltration thickness, alongside visual acuity and slit lamp examination.

Results: The mean age was 35.07 ± 6.53 years, with 43.33% male and 56.67% female. Bacterial infections (53.33%, n=16) showed significant improvement in best spectacle-corrected visual acuity (BSCVA) at 1, 2, 4, and 6 weeks ($P<0.0001$). Fungal infections (33.33%, n=10) improved at 2, 4, and 6 weeks ($P<0.0015$), while viral infections (13.33%, n=4) showed little change. Corneal thickness significantly decreased after one week, especially in bacterial infections. Infiltration thickness decreased notably for bacterial infections at 2, 4, and 6 weeks ($P<0.0001$), with no significant differences among infection types ($P>0.05$).

Conclusion: AS-OCT monitors infectious keratitis, enhancing BSCVA and lowering corneal and infiltration thickness, especially for bacterial and fungal infections. AS-OCT showed bigger bacterial infection changes, but it applied to all infections, demonstrating its role in quantitative therapy and better patient outcomes through accurate, non-invasive follow-up.

Keywords: AS-OCT; Infectious Keratitis; Corneal Imaging; Monitoring.

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Introduction

Infectious keratitis refers to a pathological condition affecting the cornea, typically caused by the presence of pathogenic microorganisms. It is a medical emergency that, if left untreated, can result in severe complications such as corneal thinning, scarring, perforation, endophthalmitis, vision loss, or even the loss of the eye **(Cabrera et al., 2022).** The etiology of keratitis can be microbial, including bacteria, fungi, and protozoa, or viral. Identifying the underlying cause is crucial for selecting the appropriate treatment plan **(Ung et al., 2019).** While initial therapy is empiric, it is essential to begin treatment immediately, as the condition can worsen rapidly. Diagnostic confirmation often takes at least 48 hours, during which any delay in treatment is associated with a poorer prognosis **(Barac et al., 2022).**

Anterior segment optical coherence tomography (AS-OCT) is a valuable tool for assessing keratitis in vivo. This imaging modality provides cross-sectional scans of the cornea, allowing for the evaluation of inflammation by measuring stromal infiltration thickness (IT) and corneal thickness (CT). AS-OCT has transformed the clinical and surgical approach to corneal diseases, offering a more detailed understanding of corneal pathology **(Abdelghany et al., 2021).** Its ability to provide both qualitative and quantitative information has proven useful in diagnosing and managing infectious keratitis caused by various pathogens. Studies have demonstrated its role in detecting infections from fungi, herpes simplex virus, cytomegalovirus, acanthamoeba, and bacteria **(Gouider et al., 2021).**

This research aims to detect changes of anterior segment optical coherence tomography in following up and prognosis of infectious keratitis.

Patients and methods

This observational, prospective, non-randomized study was conducted in the Ophthalmology Department at Qena University Hospital, South Valley University, involving 30 patients with clinically confirmed infectious keratitis. Exclusion criteria included retinal diseases such as degeneration, corneal diseases like dystrophies and ectasia, and optic nerve conditions like atrophy. The sample size was determined based on clinical findings pending culture and sensitivity results.

Our methodology included a thorough evaluation of all patients, starting with detailed history taking and visual acuity assessment, which was scored by the lowest line where at least half of the rings were correctly identified. A complete slit lamp examination was conducted with illumination provided by the slit lamp's system, performed at a 30-45° angle. The examination covered the conjunctiva, tear film, cornea, anterior chamber, iris, lens, and anterior vitreous.

All cases were diagnosed based on clinical examination and sent for culture and sensitivity, all cases treated with empirical treatment in anticipation of culture and sensitivity and then treated according to culture and sensitivity, acanthamoeba keratitis are excluded from the study.

Anterior segment Optical Coherence Tomography (OCT) was performed using the Spectralis OCT by Heidelberg Engineering (SN: TR-KT-2069, Germany), with the Heidelberg Eye Explorer software version 1.9.10.0. Vertical and horizontal raster scans (6.0-mm scan lines) were obtained, along with an add-on lens scan that provided a wider viewing angle to include the entire cornea. Corneal thickness (CT) and infiltration thickness (IT) were measured using the caliper tools within the OCT software. CT was measured at the center of the infiltration, with one caliper arm on the anterior hyperreflective corneal surface and the second arm on the hyperreflective endothelium. IT was measured at the center of the infiltration, from the anterior hyperreflective corneal surface to the posterior border of the hyperreflective area. If the posterior hyperreflective corneal surface was not visualized, CT was measured in an adjacent area, and the posterior limit of the hyperreflective infiltration was used to

measure IT. Any additional findings on OCT were recorded.

Patients were examined on presentation (day 0), and on days 7, 14, 28, and 6 weeks of treatment. The examinations included best corrected visual acuity (BCVA) using Landolt's chart, slit lamp examination, and anterior segment OCT.

Ethical approval code: SVU-MED-OPH026-1-23-8-717.

Statistical analysis

Statistical analysis was performed using SPSS version 26.0. Qualitative data were expressed as numbers and percentages, while quantitative data were summarized as mean ± standard deviation (SD). The arithmetic mean represented the central tendency, and SD measured data dispersion. Comparisons between two independent groups were conducted using the Student's t-test, with significance determined by the p-value. The Mann-Whitney test assessed differences in non-normally distributed quantitative variables, and the Chi-square test analyzed associations between categorical variables. Pearson and Spearman correlations were used to evaluate relationships between variables. A p-value < 0.05 was considered statistically significant.

Results

The general evaluation of the 30 included subjects revealed a mean age of 35.07 ± 6.53 years. The sex distribution was 43.33% male (n=13) and 56.67% female (n=17). The causative organisms were identified as bacterial in 53.33% of cases (n=16), fungal in 33.33% (n=10), and viral in 13.33% (n=4), (**Table.1).**

Table 1. General evaluation of included subjects

	Value (N = 30)
Age (Years)	35.07 ± 6.53
Sex	
Male	13 (43.33%)
Female	17 (56.67%)
Causing organism	
Bacterial	16 (53.33%)
Fungal	10 (33.33%)
Viral	4 (13.33%)

There was no significant difference between different infected groups regarding BSCVA (logMAR) (P>0.05),(**Table.2**).

Table 2. Comparison between different infected groups regarding BSCVA (logMAR)

Variables	**Bacterial Inf. Cases (N = 16)**	**Fungal Inf. Cases (N = 10)**	**Viral Inf. Cases (N = 4)**	**P. Value**
BSCVA (logMAR)				
On presentation (0)	2.14 ± 0.79	2.16 ± 0.98	1.18 ± 0.23	0.1284
	P1=0.9989, P2=0.1291, P3=0.1496			
One week	1.54 ± 0.81	1.38 ± 0.68	0.52 ± 0.17	0.0698
	P1=0.8532, P2=0.0565, P3=0.1518			
2 weeks	0.67 ± 0.72	1.05 ± 0.61	0.48 ± 0.22	0.2609
	P1=0.3552, P2=0.8688, P3=0.339			
4 weeks	0.44 ± 0.55	0.91 ± 0.83	0.46 ± 0.22	0.2055
	P1=0.1964, P2=0.9979, P3=0.4915			

6 weeks	0.28 ± 0.33	0.68 ± 0.67	0.41 ± 0.21	0.1385
	P1=0.117, P2=0.8753, P3=0.6207			

P1: Bacterial Vs. Fungal, P2: Bacterial Vs. Viral, P3: Fungal Vs. Viral

Bacterial Infections: Significant improvements in BSCVA were observed at multiple times compared to the initial evaluation. At one week, there was a significant improvement (P = 0.05) compared to the initial evaluation. This improvement continued at 2 weeks (P < 0.0001*), 4 weeks (P < 0.0001*), and 6 weeks (P < 0.0001*), all compared to the initial evaluation. Fungal Infections: Significant improvements in BSCVA were observed at several time points compared to the initial evaluation. At 2 weeks, there was a significant improvement (P = 0.0101*) compared to the initial evaluation. This improvement continued at 4 weeks (P = 0.0095*) and 6 weeks (P = 0.0015*), all compared to the initial evaluation. Viral Infections: No significant improvements were observed in BSCVA at any evaluation time point compared to the previous evaluation or the initial evaluation (P > 0.05 for all comparisons), except for post management one week evaluation. That is because viral infiltration does not cause much damage to the cornea, (**Table.3**).

Table 3. Comparison between BSCVA (logMAR) different evaluations through the study in different infected groups

	Bacterial Inf. Cases (N = 16)		**Fungal Inf. Cases (N = 10)**		**Viral Inf. Cases (N = 4)**	
	P. Previous	**P. D0**	**P. Previous**	**P. D0**	**P. Previous**	**P. D0**
One week	0.05	0.05	0.0657	0.0657	0.0073*	0.0073*
2 weeks	0.0042*	<0.0001*	0.2994	0.0101*	0.8153	0.0093*
4 weeks	0.3204	<0.0001*	0.6889	0.0095*	0.9051	0.0076*
6 weeks	0.3359	<0.0001*	0.524	0.0015*	0.7827	0.0049*

P. Previous: Comparison with previous evaluation Time, P.D0: Comparison with first evaluation Time (D0).

Upon presentation, bacterial-infected corneas had a mean thickness of 697.31 ± 62.29 µm, significantly thinner than fungal-infected corneas at 820.1 ± 96.39 µm (P = 0.0006*) and slightly thicker than viral-infected corneas at 633.5 ± 89.84 µm (P = 0.003*). By one week, all groups showed a significant decrease in corneal thickness: bacterial (650.63 ± 59.27 µm), fungal (763.9 ± 115.27 µm), and viral (587.25 ± 32.92 µm) infections (P = 0.0016*). At 2 weeks, significant differences persisted between bacterial (609 ± 60.96 µm), fungal (724.6 ± 133.84 µm), and viral (557.5 ± 21.28 µm) infections (P = 0.0053*). By 4 weeks and 6 weeks, corneal thickness continued to decrease across all groups, with significant differences observed among bacterial (590.19 ± 63.67 µm), fungal (704.3 ± 141.35 µm), and viral (545.25 ± 13.29 µm) infections at both time points (P = 0.0101* and P = 0.018*, respectively), (**Table.4**).

Table 4. Comparison between different infected groups regarding AS-OCT Corneal Thickness (µm)

Variables	**Bacterial Inf. Cases (N = 16)**	**Fungal Inf. Cases (N = 10)**	**Viral Inf. Cases (N = 4)**	**P. Value**
on presentation (0)	697.31 ± 62.29	820.1 ± 96.39	633.5 ± 89.84	0.0006*
	P1=0.003*, P2=0.37, P3=0.0022*			
One week	650.63 ± 59.27	763.9 ± 115.27	587.25 ± 32.92	0.0016*
	P1=0.0071*, P2=0.3863, P3=0.0042*			

2 weeks	609 ± 60.96	724.6 ± 133.84	557.5 ± 21.28	0.0053*
	P1=0.014*, P2=0.5978, P3=0.0156*			
4 weeks	590.19 ± 63.67	704.3 ± 141.35	545.25 ± 13.29	0.0101*
	P1=0.0216*, P2=0.6996, P3=0.0299*			
6 weeks	571.25 ± 66.12	687.7 ± 149.14	543.25 ± 18.54	0.018*
	P1=0.0263*, P2=0.8812, P3=0.067			

P1: Bacterial Vs. Fungal, P2: Bacterial Vs. Viral, P3: Fungal Vs. Viral

Bacterial Infections (N = 16): Significant changes in corneal thickness were observed at various time points compared to the initial evaluation (D0): at one week (P = 0.044*), 2 weeks (P = 0.0005*), 4 weeks (P = 0.0001*), and 6 weeks (P < 0.0001*). However, when compared to the previous evaluation (P.Previous), significant changes were noted only at 2 weeks (P = 0.0005*) and 4 weeks (P = 0.0001*); no significant changes were observed at one week (P = 0.044*) and 6 weeks (P = 0.4306). Fungal Infections (N = 10): No significant changes in corneal thickness were observed compared to either the initial evaluation (D0) or the previous evaluation (P.Previous) at one week, 2 weeks, 4 weeks, or 6 weeks (P > 0.05). Viral Infections (N = 4): Similarly, no significant changes in corneal thickness were observed compared to either the initial evaluation (D0) or the previous evaluation (P.Previous) at one week, 2 weeks, 4 weeks, or 6 weeks (P > 0.05), (**Table.5**).

Table 5. Comparison between AS-OCT Corneal Thickness (µm) different evaluations through the study in different infected groups

Variables	**Bacterial Inf. Cases (N = 16)**		**Fungal Inf. Cases (N = 10)**		**Viral Inf. Cases (N = 4)**	
	P. Previous	**P. D0**	**P. Previous**	**P. D0**	**P. Previous**	**P. D0**
One week	0.044*	0.044*	0.2766	0.2766	0.4345	0.4345
2 weeks	0.0676	0.0005*	0.5129	0.0995	0.2367	0.2038
4 weeks	0.415	0.0001*	0.758	0.0573	0.4301	0.1433
6 weeks	0.4306	<0.0001*	0.8112	0.0382*	0.8843	0.1392

P. Previous: Comparison with previous evaluation Time, P.D0: Comparison with first evaluation Time (D0)

There was no significant difference between different infected groups regarding Infiltration Thickness (µm) (P>0.05), (**Table.6**).

Table 6. Comparison between different infected groups regarding AS-OCT Infiltration Thickness (µm)

Variables	**Bacterial Inf. Cases (N = 16)**	**Fungal Inf. Cases (N = 10)**	**Viral Inf. Cases (N = 4)**	**P. Value**
on presentation (0)	239.94 ± 73.79	280.4 ± 104.55	273.25 ± 152.38	0.5997
	P1=0.6019, P2=0.8341, P3=0.9925			
One week	211.25 ± 96.62	260.5 ± 110.37	188.5 ± 103.65	0.4183
	P1=0.5028, P2=0.9248, P3=0.5054			
2 weeks	135.13 ± 115.64	239.9 ± 115.19	134.25 ± 107.67	0.099
	P1=0.0978, P2=0.9999, P3=0.316			
4 weeks	71.75 ± 104.56	155.9 ± 145.56	42.5 ± 63.65	0.1689
	P1=0.2204, P2=0.9042, P3=0.2761			
6 weeks	45.31 ± 99.55	127.8 ± 152.34	0 (0%)	0.1351
	P1=0.2231, P2=0.7805, P3=0.19			

P1: Bacterial Vs. Fungal, P2: Bacterial Vs. Viral, P3: Fungal Vs. Viral

Bacterial Infections (N = 16): Significant reductions in infiltration thickness were observed at 2 weeks (P = 0.006*), 4 weeks (P < 0.0001*), and 6 weeks (P <0.0001*) compared to baseline (D0). However, there were no significant changes compared to the previous evaluation time (P > 0.05). Fungal Infections (N = 10): No significant changes in infiltration thickness were observed at any evaluation time point compared to baseline (D0) or the previous evaluation (P > 0.05). Viral Infections (N = 4): Similarly, no significant changes in infiltration thickness were noted at any evaluation time point compared to baseline (D0) or the previous evaluation (P > 0.05), (**Table.7**).

Table 7. Comparison between AS-OCT Infiltration Thickness (µm) different evaluations through the study in different infected groups

Variables	Bacterial Inf. Cases (N = 16)		Fungal Inf. Cases (N = 10)		Viral Inf. Cases (N = 4)	
	P. Previous	P. D0	P. Previous	P. D0	P. Previous	P. D0
One week	0.3681	0.3681	0.6992	0.6992	0.4561	0.4561
2 weeks	0.0598	0.006*	0.703	0.4449	0.5527	0.2444
4 weeks	0.1259	<0.0001*	0.1914	0.0517	0.2509	0.0518
6 weeks	0.4837	<0.0001*	0.6938	0.0234*	0.2914	0.021*

P. Previous: Comparison with previous evaluation Time, P.D0: Comparison with first evaluation Time (D0)

Case Presentation

Case (1): A representative case showing progressive decrease in CT AND IT

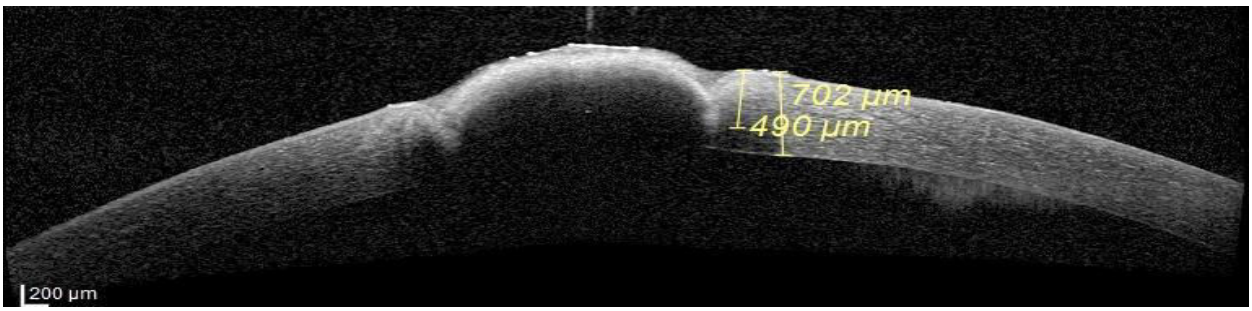

Fig.1. Day of presentation

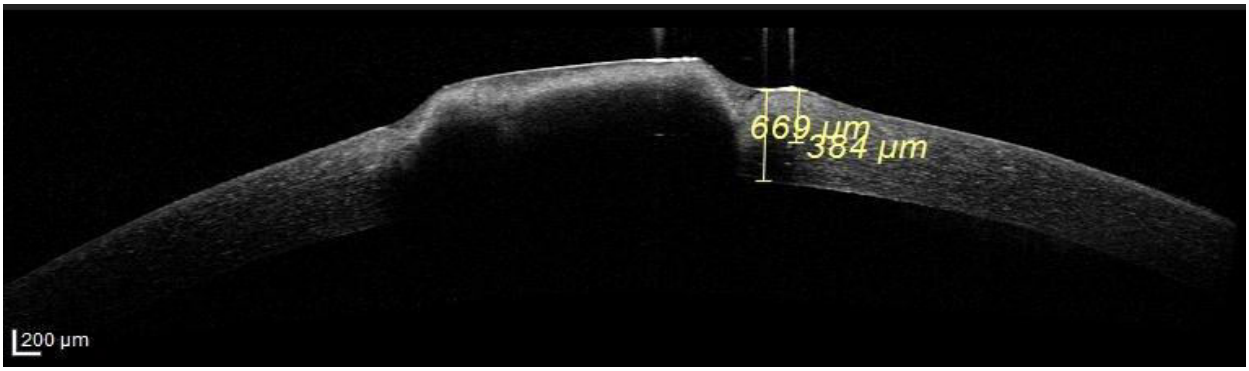

Fig.2. 7 days of presentation

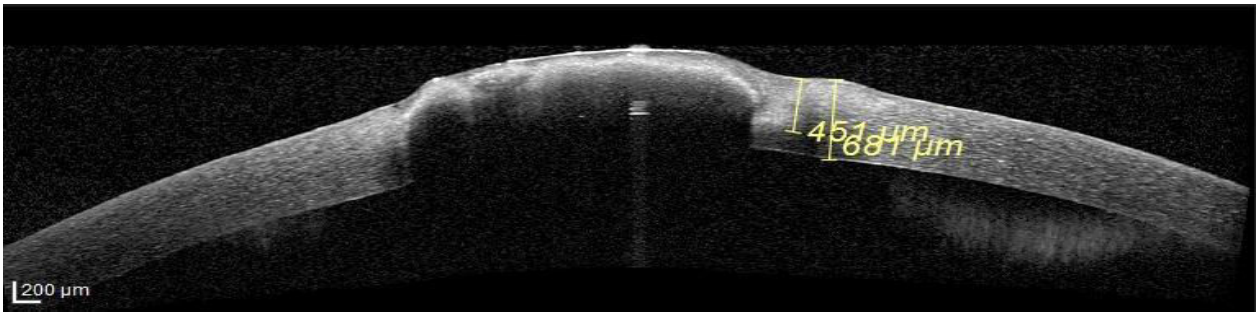

Fig.3.14 days of presentation

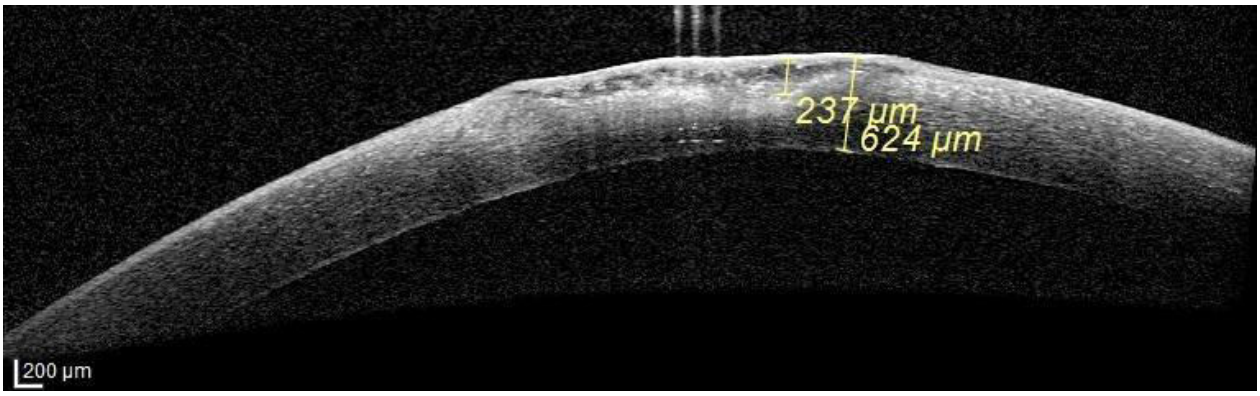

Fig.4. 28 days of presentation

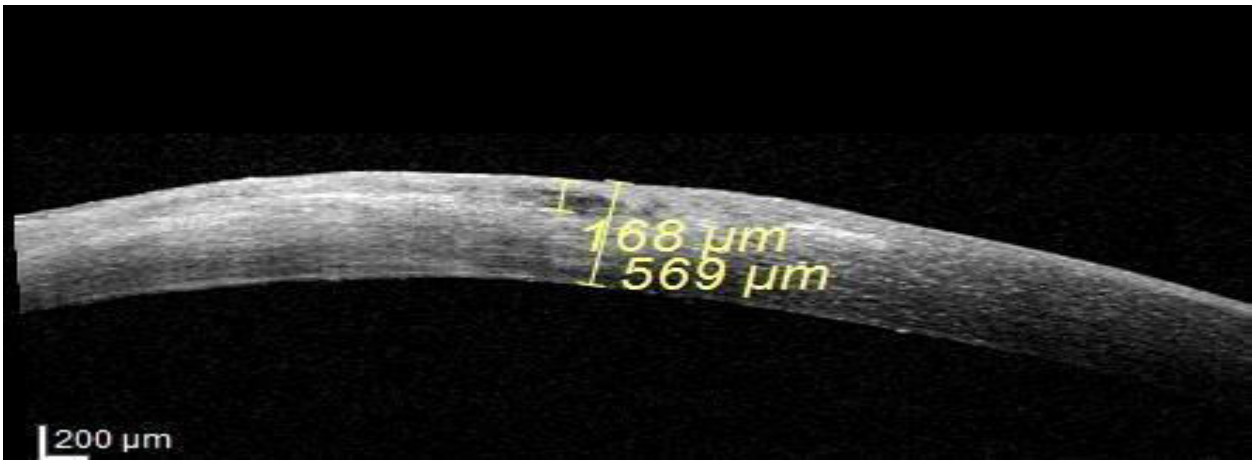

Fig.5. 6 weeks of presentation

Case (2): A representative case showing progressive decrease in CT AND IT in a case of viral corneal ulcer.

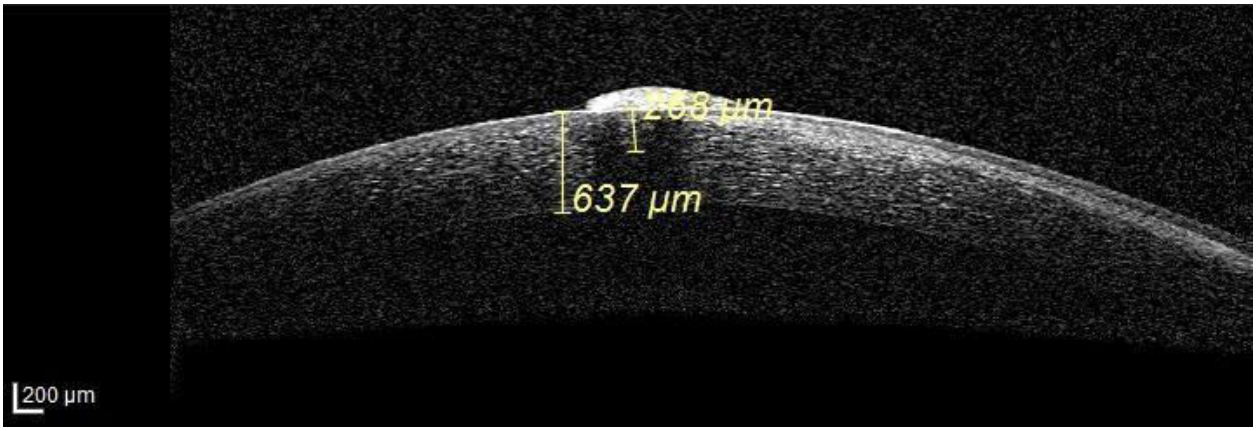

Fig.6. Day of presentation

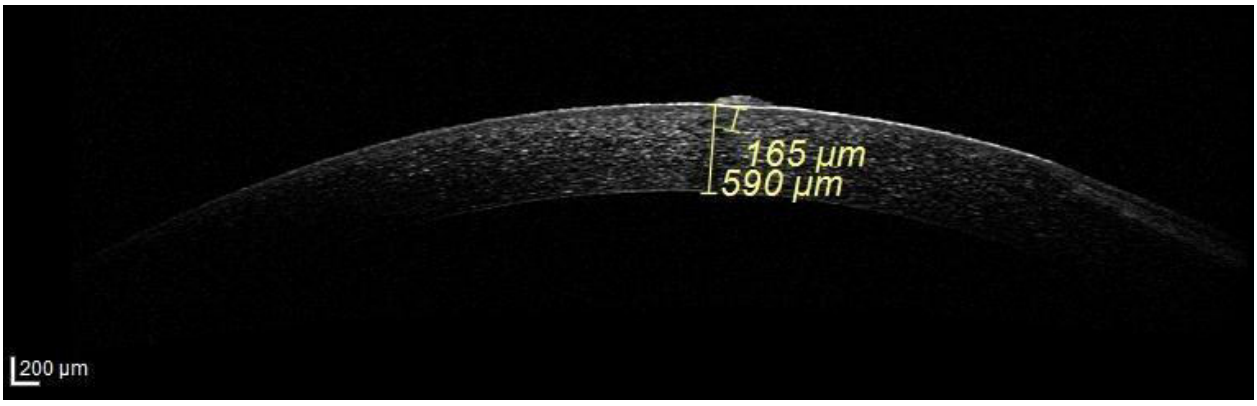

Fig.7. 7 days of presentation

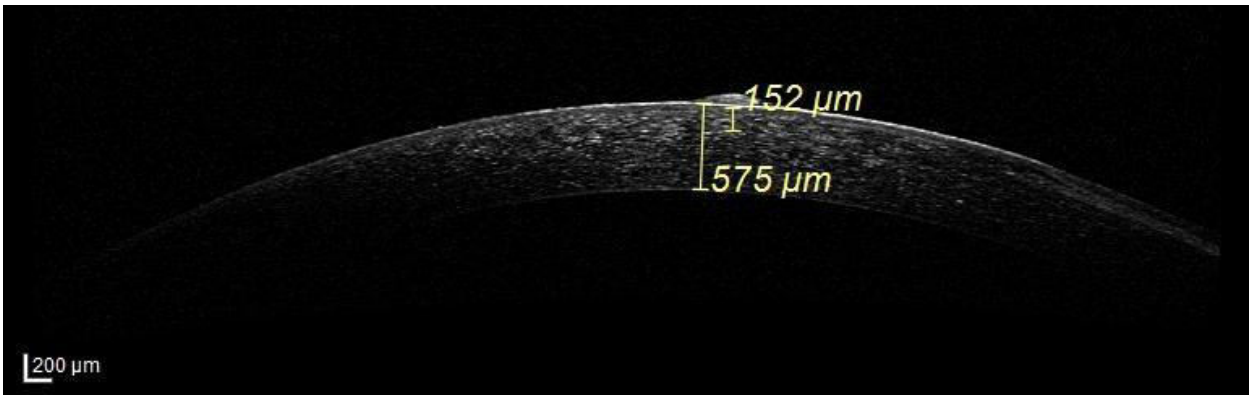

Fig.8. 14 days of presentation

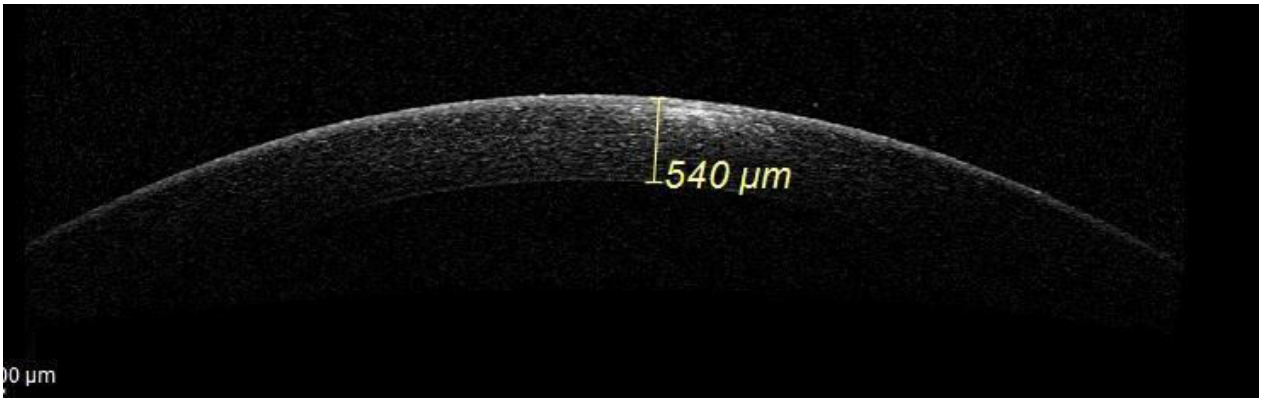

Fig.9. 4 weeks of presentation showing sub epithelial haze .

Findings other than CT AND IT:

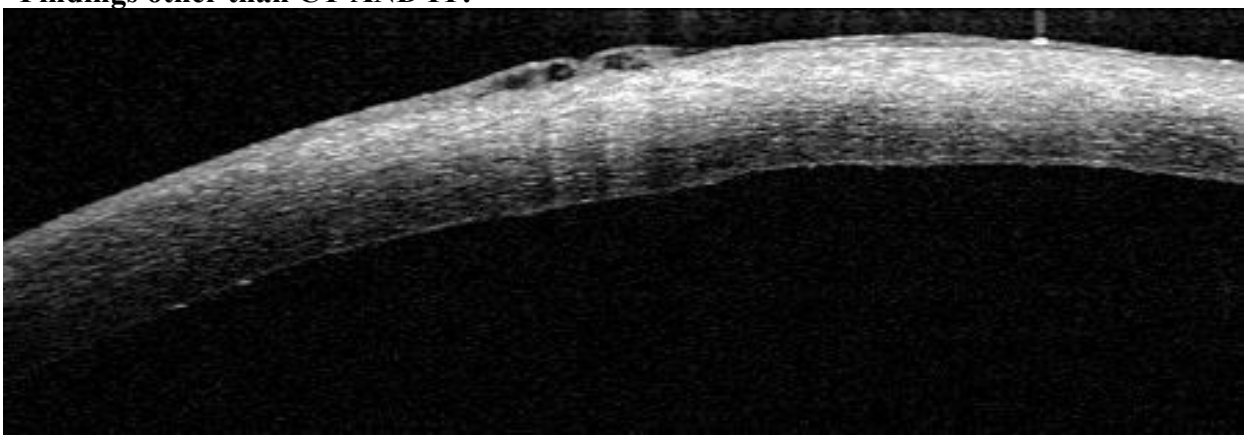

Fig.10. Epithelial cystic spaces in herpes simplex keratitis

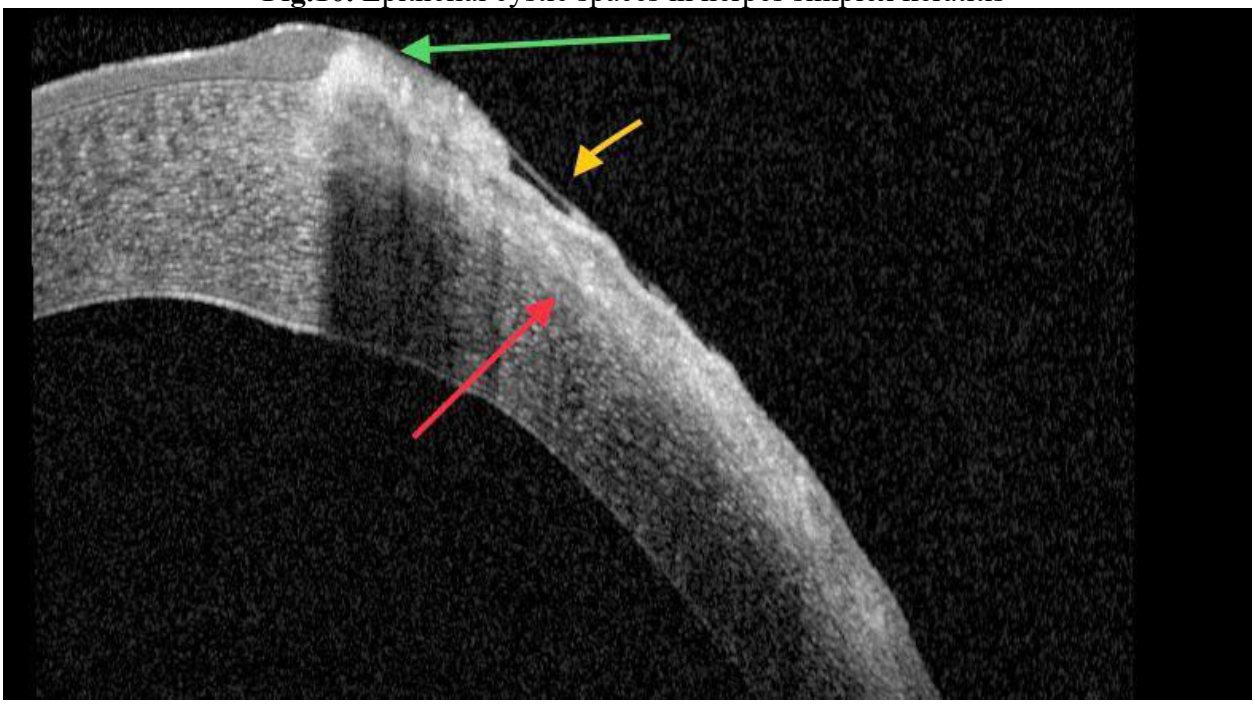

Fig.11. Anterior segment optical coherence tomography image shows hypo reflective space of tear film pool over an area of epithelial defect (yellow arrow), regenerating epithelium at the

edge pf the defect (green arrow), hyper reflective area of the anterior stroma indicating corneal scarring (red arrow)

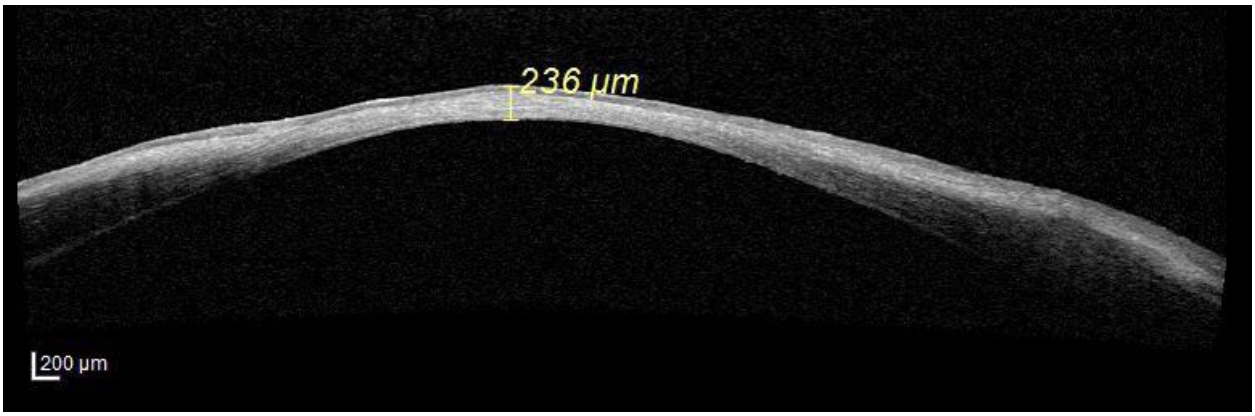

Fig.12. Corneal scar following infective keratitis showing thinned cornea

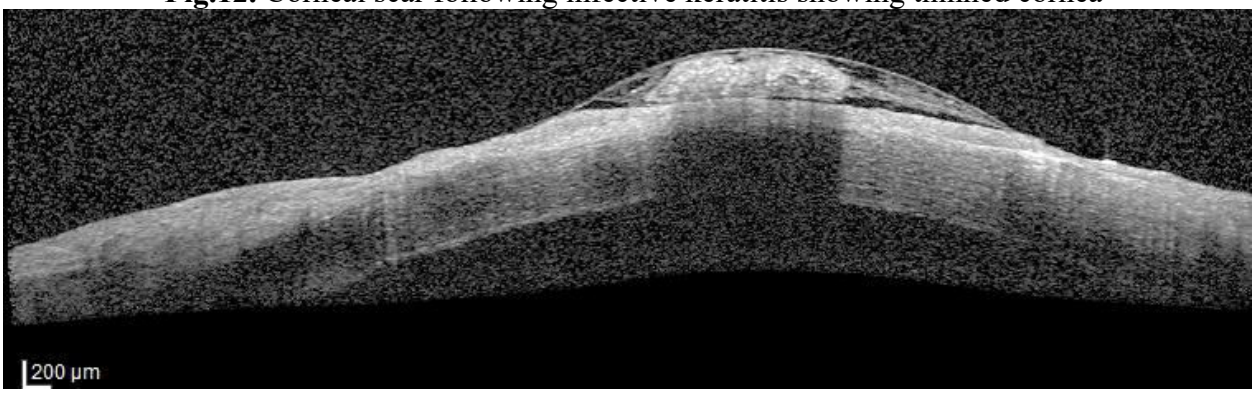

Fig.13. Hyper-reflective material representing mucous plug Overlying defective epithelium

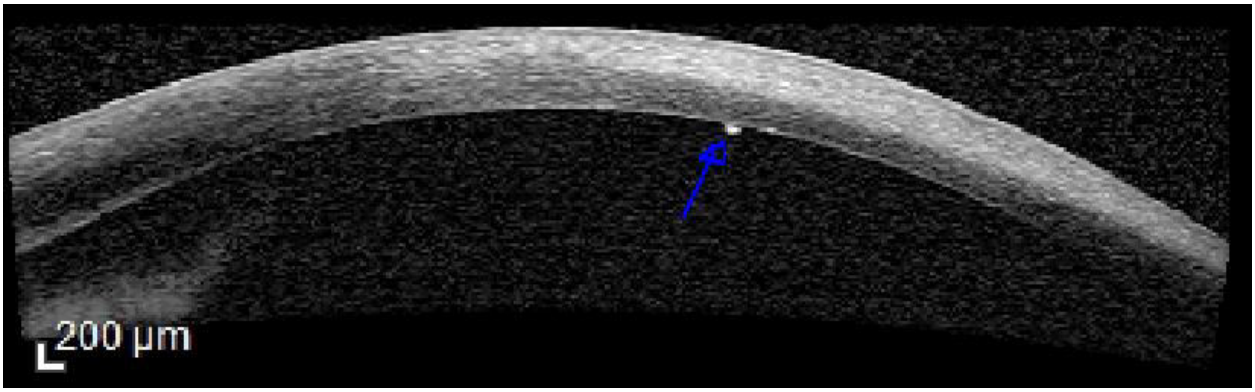

Fig.14. blue arrow shows endothelial deposits (keratic precipitate)

Discussion

In our study of 30 cases, the mean age was 35.07 years, with 43.33% male and 56.67% female. Causative organisms included bacteria (53.33%), fungi (33.33%), and viruses (13.33%). No significant differences were found among these groups. Best-corrected visual acuity (BSCVA) significantly improved from a mean logMAR of 2.02 to 0.77 after two weeks, with further, though non-significant, improvement observed at six weeks. Our study findings highlight that the most notable healing occurred in the first two weeks, emphasizing the early effectiveness of treatment in controlling infection and

initiating recovery. This early reduction in microbial load and inflammation likely contributed to continued improvement, though by four weeks, the pace of recovery slowed as most causative organisms had been eradicated **(Feizi et al., 2021).**

Significant improvements in BSCVA were seen in cases of bacterial and fungal infections over time. Bacterial infections showed progress at 1, 2, 4, and 6 weeks, while fungal infections improved at 2, 4, and 6 weeks. Viral infections, however, showed significant improvement only in one week. In bacterial infections, the significant improvement at one week is attributed to the initial eradication of the bacterial pathogen, reducing inflammation and initiating the ocular healing process.

As the treatment continued, visual acuity steadily improved, although less dramatically than in the early phase **(Sharma et al., 2021).** Another study findings also showed that fungal infections responded more slowly, with improvements linked to the prolonged treatment required to penetrate fungal cells, gradually reducing inflammation and corneal edema **(Tananuvat et al., 2021).** Viral infections exhibited minimal change in BSCVA after the initial week, likely due to the less extensive corneal damage caused by the virus, with early improvement attributed to inflammation reduction **(Kim et al., 2022).**

In our study of 30 cases, complete healing rates progressively increased, starting from 13.33% at 2 weeks, 36.67% at 4 weeks, and reaching 73.33% by 6 weeks. No complete healing was observed in the first week, as expected since the focus was on controlling the infection and preventing further damage rather than achieving full healing. By two weeks, 13.33% of cases showed healing, reflecting initial treatment effectiveness. At four weeks, 36.67% showed healing, and by six weeks, 73.33% achieved full recovery, aligning with the cumulative effects of treatment over time, similar to findings by **Cabrera et al.(2022)**.

Our study findings also showed initial mean corneal thickness at 729.73 ± 103.73 µm, with no significant changes over time. However, infiltration thickness significantly decreased at 4 weeks but remained stable at 6 weeks. Bacterial infections initially had thinner corneas compared to fungal and slightly thicker compared to viral infections, with corneal thickness significantly decreasing across all groups by week 1 and continuing to decline, with significant differences noted at 4 and 6 weeks.

The distinct differences in corneal and infiltration thickness among bacterial, fungal, and viral keratitis reflect the unique pathophysiological mechanisms of each infection. Bacterial keratitis showed rapid thinning after initial thickening, while fungal keratitis demonstrated slower reductions due to more chronic inflammation. Viral keratitis, with less severe involvement, showed a thinner cornea at baseline with steady changes over time, which supports findings by **Bonnet et al.(2020).** The thinning trend observed in our study, with corneal thickness decreasing to 606.33 ± 114.83 µm by week 6, was not statistically significant, suggesting that factors like inflammation or fluid dynamics remained stable despite effective microbial eradication, similar to **Blackburn et al.(2019)**. Infiltration thickness, initially averaging 257.87 ± 100.08 µm, showed significant reductions by 4 weeks with little change after that, indicating that most of the infiltration resolved by week 4, consistent with findings by **Matsumura et al.(2023).**

Clinically, AS-OCT allows longitudinal monitoring of anterior segment infection and inflammation. In cases of microbial keratitis, hyperreflective bands indicating acute cellular infiltration were observed on AS-OCT, along with increased corneal thickness. Monitoring the treatment response involved tracking regression of the hyper-reflective interface and changes in corneal thickness, as demonstrated by **Jiao et al.(2019).**

In our study, significant corneal thickness changes in bacterial infections were observed at 1, 2, 4, and 6 weeks, with notable reductions in infiltration thickness at 2, 4, and 6 weeks. No significant changes in corneal or infiltration thickness were noted in fungal or viral infections at any point. The early significant reduction in bacterial infections at 1 week suggests a quick response to treatment, reducing edema and inflammation. By 6 weeks, the stabilization of corneal thickness indicates that the infection had been effectively controlled and the corneal structure approached a stable state, in line with findings by **Egrilmez and Yildirim-Theveny(2020).** The lack of significant changes in fungal infections suggests that they may cause less pronounced corneal changes or that the treatment's effects are slower to manifest due to the more chronic nature of fungal keratitis, as suggested by **Harbiyeli et al.(2022).** Viral infections caused stable corneal thickness, likely due to less severe damage compared to bacterial or fungal infections, supporting the findings of **Mohan et al.(2022).**

Our study findings align with **Srinivasan et al.(2014)**, reported significant visual acuity improvement in bacterial keratitis over different time intervals, with median improvements of 2.4 log MAR lines by 3 weeks and further gains up to 12 months. These improvements support our study, which observed significant reductions in corneal thickness and infection resolution in bacterial cases.

Konstantopoulos et al.(2011), also found that corneal and infiltration thickness significantly decreased in bacterial keratitis, reporting corneal thickness reductions from 905 µm to 584 µm over 14 days, which aligns with our findings of bacterial infections stabilizing over time. However, our study differs from **Soliman et al.(2013),** who found 12 distinct AS-OCT patterns in fungal and bacterial keratitis but reported unique early localized and diffuse necrotic stromal cystic spaces in fungal cases. The discrepancy might stem from their smaller sample size and exclusion of viral keratitis, unlike our study.

Our study disagrees with **Sharma et al.(2018),** who reported significant reductions in corneal and infiltration thickness in fungal keratitis at multiple follow-up points, with corneal thickness decreasing from 650.5 µm to 522.8 µm over 42 days. Sharma et al., study included 50 eyes, all with fungal keratitis, which may explain the difference from our study, which included viral infections and a smaller sample size. Variations in the model of AS-OCT devices and alternate therapies used may also account for the differences in findings.

Conclusion

In conclusion, our study shows that AS-OCT effectively monitors and assesses infectious keratitis. Significant improvements in best spectacle-corrected visual acuity (BSCVA) were noted, especially for bacterial and fungal infections, with reductions in corneal and infiltration thickness over time. While bacterial infections exhibited more pronounced changes, AS-OCT offered valuable insights for all infection types. Despite some parameters lacking statistical significance, the overall trends affirm AS-OCT's role in providing detailed, quantitative data essential for managing infectious keratitis and improving patient outcomes through precise, non- invasive follow-up.

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