The Profile and the Treatment Outcomes of Pediatric Microbial Keratitis in a Tertiary Referral Center

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ABSTRACT

Purpose: To evaluate the predisposing factors, clinical and microbiologic features, and treatment results of pediatric microbial keratitis.

Materials and Methods: The medical records of 34 eyes with bacterial keratitis in 34 children were retrospectively reviewed. Demographic features, predisposing factors, clinical features of the infiltration, bacteriologic culture results, and treatment outcomes were analyzed.

Results: The male to female ratio was 1.8:1. The mean age at presentation was 7.3±5.5 years (0.5-16 years). The most common detectable predisposing factor was trauma (38.2%). Four (25%) of 16 cases in which corneal swaps were obtained for pathogen analyses, were culture positive. Coagulase-negative Staphylococcus was observed in three cases, and Bacillus Cereus was found in one case. The final mean best-corrected visual acuity (BCVA) was increased significantly compared to the initial BCVA (Z=-2.9, p=0.004). The risk factors leading to poor visual outcomes were initial poor BCVA, deep stromal infiltration, and hypopyon existence at presentation (R=-0.60 and p=0.01, R=-0.55 and p=0.02, R=0.80 and p<0.001, respectively).

Conclusion: The most common identifiable risk factor for childhood microbial keratitis was corneal trauma. The most common bacteria isolated were coagulase-negative Staphylococcus. Initial poor BCVA, deep stromal infiltration, and hypopyon existence at presentation were predictive for poor visual outcome. Early diagnosis, and intensive drug therapy, may effectively improve the prognosis of pediatric microbial keratitis.

Keywords: Pediatric keratitis, Bacterial keratitis, Turkey.

INTRODUCTION

Microbial keratitis is one of the leading causes of blindness worldwide.[1] The management of bacterial keratitis is somewhat different in pediatric cases compared to adults. The poor expression of the complete medical history and complaints, as well as lack of compliance in ophthalmologic examination and treatment, are some of the difficulties that the clinicians faced in pediatric cases.[2] Due to these circumstances, delay in the diagnosis and treatment might induce a challenge in the management of pediatric cases, thus leading to severe visual impairment. The results of published studies on pediatric microbial keratitis showed that there were various predisposing and etiologic factors in different geographical locations.[3,4,5,6]

In this study, we reviewed thirty-four cases of pediatric microbial keratitis. The predisposing factors, clinical and microbiologic features, treatment modalities, and visual outcomes, along with the predictive factors in final poor vision, were discussed.

MATERIAL AND METHODS

Study Design

This retrospective study was conducted at Van Yuzuncu Yil University, Faculty of Medicine, between March 2020 and May 2020. Approval from the Institutional Ethics Board was obtained before conducting the study. Patient consent was not required due to the retrospective nature of the study. The study followed the tenets of the Declaration of Helsinki.

The medical records of thirty-four eyes of 34 patients with microbial keratitis aged 16 years or younger who were admitted to Van Yuzuncu Yil University, Faculty of

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Received: 14.09.2020
Accepted: 25.12.2020

Glo-Kat 2021; 16:31-36

DOİ: 10.37844/glauc.cat.2021.16.6

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Medicine from January 2012 through December 2018, were retrospectively reviewed. The inclusion criteria were the presence of stromal infiltration with a corneal epithelial defect staining with fluorescein and purulent discharge. The microbiologic investigations (Gram staining, culture, and antibiogram) were conducted in each one of the participants having corneal infiltration larger than 3 mm in diameter. Although culture remains the essential diagnostic tool, the cases with negative culture results were included if the case history, clinical findings, and treatment response were consistent with the diagnosis of an infectious ulcer.[4,5] The medical records were reviewed, and the following properties of the patients were noted: Gender, age, laterality, risk factors, major symptoms during the admission, duration of complaints, the concurrence of any systemic or ocular disease, best-corrected visual acuity (BCVA) at the initial visit, clinical aspects of the keratitis, culture results, treatment protocol, treatment duration (≤1 month and >1 month), follow-up duration (months) and the last follow-up corneal state along with final BCVA.

Clinical evaluation of the patients included Snellen visual acuity assessment (If the patients were able to express his/her vision) and slit-lamp examination for determination of the dimensions, depth, and location of the corneal infiltrate as well as the presence of hypopyon. The corneal infiltration was classified as ≤3 mm, 3-6 mm, and ≥6 mm according to its diameter. The depth of the infiltrate was also classified as superficial stromal (<1/3 of stromal invasion), mid-stromal (1/2-1/3 of stromal invasion), and deep stromal (>1/2 of stromal invasion). The location of the infiltration was categorized as peripheral, paracentral, and central.

Corneal swab samples were taken with sterile serum physiologic wetted swabs. After applying local anesthetic drops, scraping samples were taken from the edge of the lesion or ulcer with a sterile 22 gauge needle, and the samples were delivered to the laboratory within 15 minutes at room temperature.

Monotherapy and combined antibiotic therapy were used in the treatment of patients. Small infiltrates having ≤3 mm diameter were initially treated with topical quinolone derivative antibiotics (Moxifloxacin 5 mg/mL, hourly). If there were an insufficient response, the treatment was switched to combination therapy. Larger infiltrates (>3 mm), infiltrates invading beyond the superficial one-third of the corneal stroma and/or cases with anterior chamber reaction were classified as severe cases and treated with combined topical fortified antibiotics. Gentamicin (1.5%), cefazolin (5%), vancomycin (5%), and ceftazidime (5%) was used in the combination therapy. Cefazolin and vancomycin were combined with gentamycin and ceftazidime, respectively. The antibiotic treatment was administered promptly rather than waiting for the culture results to emerge. If the clinical response was unsatisfactory, the treatment was modified according to the culture and antibiogram results.

Statistical Analyses

Statistical analyses were performed using the SPSS software version 22 (SPSS Inc, Chicago, IL). The variables were investigated using the Kolmogorov–Smirnov test to determine their distribution. Descriptive analyses were presented using means and standard deviations for variables. A linear regression analysis was applied. The predictive factors comprising initial BCVA, the corneal infiltration diameter at baseline, the depth of the infiltrate, the location of the infiltration, and hypopyon existence at the presentation on the last follow-up visit BCVA were analyzed. A *p*-value of less than 0.05 was considered statistically significant.

RESULTS

Demographics

Thirty-four patients met the inclusion criteria of this study. A total of twenty-two (64.7%) of the patients were male, and twelve (35.3%) were female. The right eye was involved in 15 cases (44.1%) and the left in 19 (55.9%). All patients had unilateral keratitis. The mean age of the patients was 7.3±5.5 years (0.5-16 years) at presentation.

Predisposing factors

A predisposing factor was not identified in the majority of the patients (n=18, 53%). Additionally, the most common predisposing factor for microbial keratitis in the study population was ocular trauma (n=13, 38.2%), followed by ocular diseases such as blepharitis and atopic conjunctivitis (n=3, 8.8%).

Microbiologic analysis

As mentioned earlier, the infiltrations having a diameter larger than 3 mm were undergone microbiologic investigation (16 eyes of 16 patients). The culture of corneal scrapings returned positive in four eyes of sixteen patients (25%). Bacterial isolates were observed in all culture-positive cases. Gram-positive cocci were determined in three cases as coagulase-negative Staphylococcus, and a gram-positive rod was determined in one case as Bacillus Cereus.

Medical history and clinical features of the patients

The complaint duration at the initial visit was ≤7 days in the majority of the cases (n=25, 73.5%). The dominant

symptoms during the admission were redness (n=21, 62%) followed by pain (n=9, 26.5%). Central corneal ulceration with the epithelial defect was observed in all cases. The diameter of the infiltrate was ≤3 mm in 18 eyes (52.9%), between 3 and 6 mm in 13 eyes (38.2%), and ≥6 mm in 3 eyes (8.8%). The depth of the infiltration in the majority of cases was superficial (n=23, 67.6%) followed by mid-stromal (n=7, 20.6%) and deep stromal (n=4, 11.8%). Hypopyon was observed in nine eyes (26.5%) at presentation (Table 1) (Figure 1).

Treatment outcomes and predictive factors affecting the final visual outcome

All of the patients were treated with topical antimicrobial medication therapy. All keratitis was resolved with topical medication alone, and no other interventions were required during the follow-up. Eighteen eyes (52.9%) were treated with fortified cefazolin and gentamicin combination drops, and vancomycine and ceftazidime combination was administered in six eyes (17.6%). Quinolone derivative antibiotics were sufficient in the remaining cases (n=10, 29.4%) in order to treat keratitis. Treatment duration was ≤ one month in the majority of cases (n=28, 82.4%). The treatment needed to be extended beyond one month in six cases (17.6%).

Table 1: *Presentation features of the patients having bacterial keratitis.*

Demographic features, medical history aspects of the patients and infiltrate characteristics	n=34 (%)
Gender	
Male	22 (64.7%)
Female	12 (35.3%)
Laterality	
Right	15 (44.1%)
Left	19 (55.9%)
Predisposing Factors	
Unidentified	18 (53%)
Ocular Trauma	13 (38.2%)
Blepharitis	2 (5.9%)
Atopic Conjunctivitis	1 (2.9%)
Ocular Symptoms	
Redness	21 (61.8%)
Pain	9 (26.5%)
Discharge	2 (5.9%)
Photophobia	1 (2.9%)
Blurring	1 (2.9%)
Complaint Duration at presentation	
≤ 7 days	25 (73.5%)
7-14 days	3 (8.8%)
≥ 14 days	6 (17.7%)
Dimensions of the infiltrate	
≤ 3 mm	18 (53%)
3-6 mm	13 (38.2%)
≥ 6 mm	3 (8.8%)
Infiltration depth	
Superficial	23 (67.6%)
Mid-stromal	7 (20.6%)
Deep Stromal	4 (11.8%)
Infiltration location	
Central	7 (20.6%)
Paracentral	21 (61.8%)
Peripheral	6 (17.6%)
Hypopyon existence at presentation	
Present	9 (26.5%)
Absent	25 (73.5%)

The BCVA was able to be taken in seventeen patients (50%). The mean final BCVA was 0.5±0.4 (range 0.05-1.0) in decimals. After a mean follow-up of 5±6 months (range 3-33 months), all infiltrations were resolved leaving corneal scars in various diameters, and the final mean BCVA was increased significantly compared to the initial BCVA (Z=-2.9, p=0.004) (Table 2). Eight eyes (47%) achieved ≥20/40 of BCVA at the last visit. In linear regression analyses, the predictive factors were found to be the infiltration depth, hypopyon existence at presentation, and the initial BCVA in anticipating the final visual outcome (R=-0.60 and p=0.01, R=-0.55 and p=0.02, R=0.80 and p<0.001, respectively) (Table 3).

CONCLUSION

Bacterial keratitis is one of the leading causes of blindness in developing countries.[1] The incidence, responsible pathogens, and predisposing factors of bacterial keratitis were variable depending on the diverse features of the populations such as socioeconomic state, geographic aspects, and climate conditions.[2-10] To facilitate the prevention and the management of bacterial keratitis, one should know the predisposing factors, pathogens spectrum, and the predictive factors in different populations. To the best of our knowledge, this is the first study elucidating the features and outcomes of bacterial keratitis in children from Turkey.

The leading identifiable predisposing factor for pediatric bacterial keratitis was reported as ocular trauma in different studies, ranging from 27.3% to 69%.[2,3,5,6,11,12,13,14,15] Our study was in line with the current literature, and 38.2% of the cases had a history of ocular trauma at presentation. Contact lens wear was also suspected as a major risk factor for leading childhood bacterial keratitis in developing countries, especially in Taiwanese children.[3,4,6] This might be due to the high prevalence of contact lens use due to myopia in far-east countries. In contrast to this report, there were no contact lens users in our cohort, similar to the previous studies reported from China and India that contact lens wear was a negligible predisposing factor in

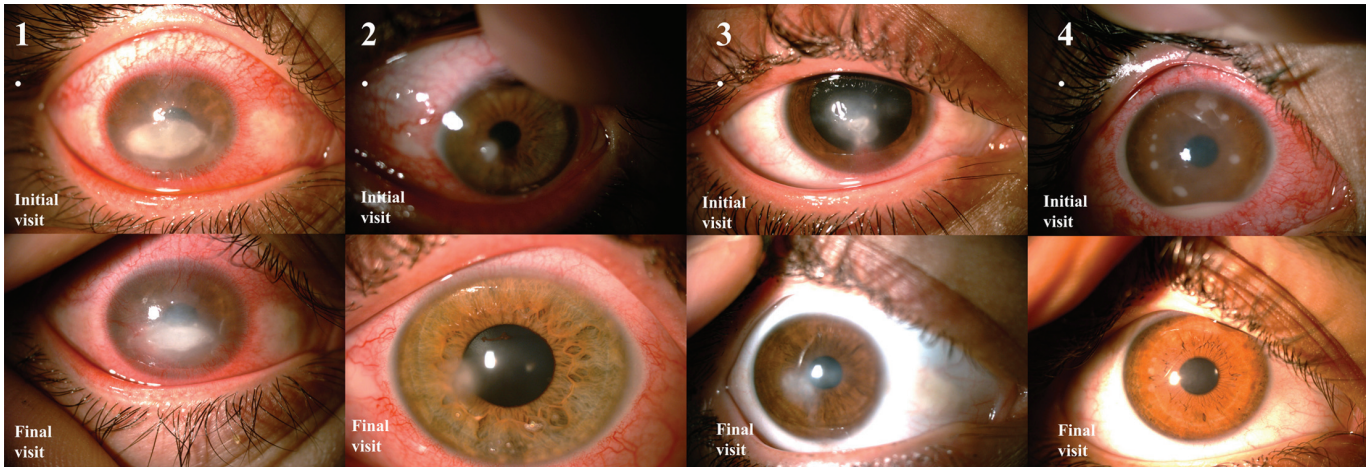

Figure 1. *The pre- and post-treatment pictures of four consecutive patients. In the first case, note the regression of infiltration along with encroaching corneal vascularization toward the infiltration. Note the dramatic regression of the infiltrate after proper topical antibiotic treatment leaving stromal scars in the second and third cases. The 4th case had multiple superficial infiltrations with hypopyon. All infiltrates had resolved after intense topical antibiotherapy leaving minimal corneal scars, and hypopyon was resolved entirely.*

Table 2: *Comparison analysis of the visual acuity in patients.*

Clinical aspects of the patients	
Parameters	**mean±SD (range)**
Age (years)	7.3 ± 5.5 (0.5-16)
BCVA at presentation (Decimals)	0.27 ± 0.27 (0.05-1.0)
Final BCVA (Decimals)	0.5 ± 0.4 (0.05-1.0)
Follow-up duration (months)	5 ± 6 (3-33)
Paired samples comparison analysis	**p-value**
Final BCVA – Initial BCVA	0.004 (Z=-2.9)

Abbreviations: **SD:** Standard deviation, **BCVA:** Best-corrected visual acuity

Table 3: *The predictive factors in anticipating final BCVA (Linear regression analyses).*

	Coefficients[a]	
	Standardized Coefficients	
Parameters	Beta	p-value
The complaint duration	-0.226	0.382
The dimension of the Lesion	-0.369	0.145
Infiltration Depth	-0.603	**0.010**
Infiltration Location	0.243	0.347
Hypopyon Excistence	-0.551	**0.022**
BCVA at presentation	0.804	**<0.001**

a. Dependent Variable: Final BCVA

Abbreviations: **BCVA:** Best-corrected visual acuity.

the development of pediatric microbial keratitis.[2,5,12,16,17] We could not have found a predisposing factor in the 53% of our cohort. Similarly, in a retrospective study evaluating the keratitis cases associated with various microorganisms, Budak BA et al. also could not have found any predisposing factor in the majority of the cases (62.5%).[14] In a large cohort comprising 138 eyes with bacterial keratitis, the dominant symptom at presentation was reported to be redness followed by discharge.[18] Based on our results, similar to the previous reports, redness was the major presenting symptom in patients having bacterial keratitis. The second most common symptom was ocular pain in our cohort. The mean duration of symptoms at presentation was previously reported as 11.5 days in a large cohort.[18] Song et al. reported that most of the pediatric cases with bacterial keratitis (43.8%) applied to their clinic during the first week of the symptoms.[2] In our study, the majority of cases (73.5%) were also admitted in the first week of symptoms.

The location, depth, and dimension of the infiltrations vary in different studies.[2,19] Song et al. reported that 85% of the infiltrations were located in the central cornea in their cohort, the majority of the lesions had a dimension between 3 to 6 mm, and the depth of the infiltration invasion to the corneal stroma was superficial in 41.3% of cases. Hypopyon was seen in 31.3% of patients in the same study.[2] Lee et al. reported that 48.5% of keratitis cases that seen between 2008-2012 were located paracentral cornea and the dimensions were dominantly medium in size (51.5%).[19] In our series, infiltration was located in the paracentral cornea in 61.8% of cases, infiltration depth was generally superficial, and the diameter of the lesion was mostly equal or smaller than 3 mm. Additionally, similar

to the previous report, hypopyon was present in 26.5% of cases at presentation.[2]

The culture positivity rate was 25% in our case series. It was lower than those previously reported on childhood bacterial keratitis, which was ranging between 56.6% to 87%. The reason for this outcome might be due to prior antimicrobial therapies. The studies conducted in China and India showed that the predominant bacterial isolates were coagulase-negative Staphylococcus.[2,5,17] In contrast to these reports, Pseudomonas aeruginosa, a gram-negative bacteria, was found to be most prevalent in the United States and Taiwan.[3,4,11] In our series, keeping in mind the low percentage of positive cultures, the most common isolate was coagulase-negative Staphylococcus, similar to the India region. In our study, intensive antibiotic treatment was given in all eyes, and the resolution of active infiltrate was seen eventually. Prolonged treatment duration was warranted in a minor percentage of cases (17.6%). In the literature, a small percentage of eyes varying from 5.6 to 26.2% needed surgical intervention due to a lack of sufficient response to medical treatment.[2-6,20] We had no need for surgery in our cohort, and we thought the reason was the absence of fungal keratitis in our cohort and the predominance of superficial and small infiltrates.

Visual acuity, as anticipated, could not be acquired due to a lack of expression of vision in some patients (n=17). Besides, we achieved a statistically significant BCVA improvement in those who had a visual expression, after a mean follow-up of 5±6 months (range 3-33 months) (Z= -2.9, p=0.004). In a study comprising 107 children with bacterial keratitis, Rosetto et al. also reported a significant improvement in BCVA after a mean follow-up of 40.6 ± 91.6 weeks (p<0.001).[21] Young et al. reported that a best-corrected visual acuity (BCVA) of ≥20/40 was achieved in 13 out of 17 eyes (76.5%) at the last follow-up.[20] Hsiao et al. reported that thirty-three eyes of 68 eyes (48.5%) had BCVA of 20/25 or better at the last follow-up.[4] In our series, 47% of patients who were able to express visual acuity had BCVA of 20/40 or better at the last follow-up. In linear regression analysis, the initial poor BCVA, deep stromal infiltration, and hypopyon existence at presentation were found to be predictive in the final poor BCVA in our study. Lee et al. also reported that initial poor BCVA was significantly associated with the final poor BCVA.[19] Additionally, they have pointed out that young age, along with gram-negative bacteria infection, particularly Pseudomonas, was also highly predictive for poor visual outcomes. In our series, deep stromal infiltration along with hypopyon existence were found to be predictive for poor visual outcome, presumably due to the aggressive nature of the pathogen in these cases.

In conclusion, bacterial keratitis had great importance in childhood due to its potential effects on constant visual disturbance. In our series, the majority of patients were applied to our clinic with a complaint of redness in the first week of the infection. Infiltration was located in the paracentral cornea in the majority of cases, infiltration depth was generally superficial, and the diameter of the lesion was mostly equal or smaller than 3 mm. All patients were treated with topical antibiotics, and no surgical intervention was warranted. BCVA was improved significantly, and the risk factors leading to poor visual outcomes were initial poor BCVA, deep stromal infiltration, and hypopyon existence at presentation.

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