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Correlation between clinical and laboratory culture findings in resistant keratitis

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Abstract

Background: The clinical diagnosis of infective keratitis does not give an unequivocal indication of the causative organisms because a wide range of organisms can produce a similar clinical picture. The causative agents of infective keratitis frequently isolated are: bacteria, fungi, viruses and Parasites.

Aim and Objectives: The purpose of this study was to identify the correlation between clinical and culture laboratory finding in resistant keratitis at the Ophthalmology Department of Tanta University Hospitals.

Subjects and Methods: This study was a prospective interventional selectively randomized clinical study which extended for 12 months at Tanta university hospitals and included fifty eyes of fifty patients clinically diagnosed resistant keratitis and presenting to The Ophthalmology Department of Tanta University Hospitals. The study started in January 2021.

Results: there was statistically significant deference between groups regarding to Medical history, Trauma, Ulcer characteristics, Satellite lesions and corneal sensation. There was no statistically significant deference between groups regarding to age, gender, Contact wearing, foreign body, Ulcer size and gutter and immune ring.

Conclusion: Clinical diagnosis is more important for treatment and follows up while culture is performed for documentation of the clinical findings. Incidence of fungal keratitis is significantly high in our region. The therapeutic approach can initially be based on clinical impression and evidence of the microbiologic trends of infectious keratitis and sensitivity/resistance patterns in our locality.

Keywords: Clinical, laboratory culture findings, resistant keratitis

Introduction

Around the world, infectious keratitis is a significant, preventable etiology of monocular blindness ^[1].

Since a variety of organisms may generate a similar clinical presentation, the clinical diagnosis of infective keratitis does not provide a clear demonstration of the causative organisms ^[2].

The two significant, frequently applied microbiological investigations. based on the clinical and microbiological assessment, immediate antibiotic therapy must be started in order to reduce ocular morbidity ^[1].

The causative agents of infective keratitis frequently isolated are: bacteria, fungi, viruses and Parasites ^[3].

Patients and Methods

This study was a prospective interventional selectively randomized clinical study which extended for 12 months at Tanta university hospitals and included fifty eyes of fifty patients clinically diagnosed resistant keratitis and presenting to The Ophthalmology Department of Tanta University Hospitals. The study started in January 2021.

Inclusion criteria: All patients with clinical findings of resistant keratitis, presenting at Tanta hospital during the study period, was included and as bacterial, fungal, neurotrophic ulcers, Mooren's ulcer, and peripheral ulcerative keratitis.

Exclusion criteria: Suspected viral Keratitis and Acanthamoeba Keratitis were excluded and also, patient with severe corneal thinning were excluded.

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Patient evaluation: All study participants underwent: A comprehensive of history, Full ophthalmic examination and Corneal scrapings.

Culture: The obtained specimens were subjected to both microbiological culture and sensitivity testing.

Ethical considerations

Study protocol was submitted for approval by the Ethical Committee of faculty of medicine - Tanta University. The data that were obtained from participants are confidential. The study participants will not be identified by name in any report or publication concerning this study. Before the participants were admitted in this study, the purpose and nature of the study, as well as the risk-benefit assessment was explained to them. An informed consent was obtained.

Statistical analysis

With the aid of the IBM SPSS software package version 20.0, data were fed into the computer and evaluated. (IBM Corp, Armonk, NY). Number and percentage were used to describe qualitative data. The normality of the distribution was examined using the Kolmogorov-Smirnov test. The range (minimum and maximum), mean, standard deviation (SD), median, and interquartile range (IQR) were used to characterise quantitative data. The significance of the findings was assessed at the 5% level.

Results

Patients were divided and compared according to clinical diagnosis into five groups:

Group I: Included 7 participants with bacterial ulcer.

Group II: Included 35 patients with fungal ulcer.

Group III: Included 2 patients with mooren ulcer.

Group IV: Included 4 patients with neurotrophic ulcer.

Group V: Included 2 patients with PUK ulcer.

Age and gender were insignificantly different among the studied groups. Medical history was susta the studied groups (P value<0.001). Table (1)

The incidence of trauma was significantly different between all studied groups (P value=0.040), it was higher in fungal group compared to neurotrophic group (P value = 0.047), while it was insignificant among bacterial, mooren and PUK

groups. 1 (14.3%) patient in bacterial group, 6 (17.1%) patients in fungal group were wearing contacts. Number of patients wearing contacts was insignificantly different among the studied groups. 1 (14.3%) patient in bacterial group, 2 (5.7%) patients in fungal group and no patients in mooren, neurotrophic or PUK groups had foreign bodies. The presence of foreign bodies was insignificantly different among the studied groups. Ulcer size ranged from 1 to 4 mm with a mean (±SD) 2.21±0.906 mm in bacterial group, and from 1 to 5 mm with a mean (±SD) of 2.91±1.067 mm in fungal group, and from 1 to 2 mm with a mean (±SD) of 1.50±0.707 mm in mooren group, size of all neurotrophic ulcers was 2 mm, and from 2 to 3 mm with a mean (±SD) of 2.50±0.707 mm in PUK group. Ulcer size was insignificantly different among the studied groups. Table (2) Regarding depth of ulcer, there was a significant difference between bacterial group in comparison to fungal, mooren, neurotrophic and PUK groups (P value <0.05). There was no significant difference among fungal, mooren, neurotrophic and PUK groups. Regarding edge of ulcer, there was a significant difference between bacterial group in comparison to fungal group (P value <0.001), and between fungal group in comparison to mooren, neurotrophic and PUK groups (P value<0.05). Number of patients who had feathery ulcer edge in fungal group was significantly higher than other groups (P value<0.001). Regarding bed of ulcer, there was a significant difference between fungal group in comparison to neurotrophic group (P value<0.001) but there was no significant difference among other groups. Table (3) 27 (77.1%) patients in fungal group, and 1 (50%) in PUK group had satellite lesions. 15 (42.9%) patients in fungal group had gutter and immune ring. Regarding satellite lesions, there was a significant difference between fungal group in comparison to bacterial and neurotrophic groups (P value <0.001 and P value=0.006 respectively) but there was no significant difference between other groups. The incidence of satellite lesions in fungal group was significantly higher than other groups. Gutter and immune ring was insignificantly different among the studied groups. Table (4)

The incidence of diminished corneal sensation in neurotrophic group was significantly higher than bacterial and fungal groups (P value< 0.05). Table (5).

Table 1: Demographic data of the studied groups

		Bacterial (n=7)	Fungal (n=35)	Mooren (n=2)	Neurotrophic ulcer (n=4)	PUK (n=2)	P-value
Age (years)	Mean ± SD	41.86±14.71	48.40±12.18	59.50±3.54	46.50±4.2	53±5.66	0.406
	Range	26 - 65	27 - 70	57 - 62	42 - 51	49 - 57	
Gender	Male	4 (57.1%)	19 (54.3%)	1 (50%)	1 (25%)	1 (50%)	0.858
	Female	3 (42.9%)	16 (45.7%)	1 (50%)	3 (75%)	1 (50%)	
Medical history	DM	2 (28.6%)	11 (31.4%)	0 (0%)	1 (25%)	0 (0%)	<0.001*
	Rheumatoid arthritis	0 (0%)	0 (0%)	0 (0%)	3 (75%)	0 (0%)	

*: Statistically significant as P value < 0.05, PUK: Peripheral ulcerative keratitis, DM: Diabetes mellitus.

Table 2: Trauma, Contact wearing, Foreign body and Ulcer size (mm) of the studied groups

	Bacterial (n=7)	Fungal (n=35)	Mooren (n=2)	Neurotrophic ulcer (n=4)	PUK (n=2)	P-value
Trauma	5 (71.4%)	20 (57.1%)	0 (0%)	0 (0%)	0 (0%)	0.040*
P1		0.681	0.167	0.061	0.167	
P2			0.204	0.047*	0.204	
P3				---	---	
P4					---	
Contact wearing	1 (14.3%)	6 (17.1%)	0 (0%)	0 (0%)	0 (0%)	0.811
Foreign body	1 (14.3%)	2 (5.7%)	0 (0%)	0 (0%)	0 (0%)	0.850
Ulcer size (mm)	2.21±0.906	2.91±1.067	1.50±0.707	2.00±0.000	2.50±0.707	0.104
	1 - 4	1 - 5	1 - 2	2 - 2	2 - 3	

*: Statistically significant as P value < 0.05, PUK: Peripheral ulcerative keratitis, P1: P values compared to bacterial group, P2: P values compared to fungal group, P3: P values compared to mooren group, P4: P values compared to neurotrophic group.

Table 3: Ulcer characteristics of the studied groups

		Bacterial (n=7)	Fungal (n=35)	Mooren (n=2)	neurotrophic ulcer (n=4)	PUK (n=2)	P-value	
Depth of ulcer	<20%	7 (100%)	3 (8.6%)	0 (0%)	1 (25%)	1 (50%)	<0.001*	
	20-50%	0 (0%)	22 (62.9%)	1 (50%)	2 (50%)	1 (50%)		
	>50%	0 (0%)	10 (28.6%)	1 (50%)	1 (25%)	0 (0%)		
	P1		< 0.001*		0.011*	0.027*		0.047*
	P2				0.773	0.589		0.163
		P3				0.687	0.367	
		P4				0.687		
Edge of ulcer	Rounded	5 (71.4%)	5 (14.3%)	2 (100%)	2 (50%)	1 (50%)	<0.001*	
	Feathery	0 (0%)	28 (80%)	0 (0%)	0 (0%)	0 (0%)		
	Serrated	2 (28.6%)	2 (5.7%)	0 (0%)	2 (50%)	1 (50%)		
	P1		< 0.001*		1.000	0.576		1.000
	P2				0.011*	0.002*		0.022*
		P3				0.467	1.000	
		P4				1.000		
Bed of ulcer	Clean	1 (14.3%)	0 (0%)	0 (0%)	3 (75%)	0 (0%)	<0.001*	
	Stromal infiltrated	6 (85.7%)	35 (100%)	2 (100%)	1 (25%)	2 (100%)		
	P1		0.167		1.000	0.088		1.000
	P2				---	<0.001*		---
	P3							0.4
		P4				0.4		

*: Statistically significant as P value < 0.05, PUK: Peripheral ulcerative keratitis, P1: P values compared to bacterial group, P2: P values compared to fungal group, P3: P values compared to mooren group, P4: P values compared to neurotrophic group.

Table 4: Satellite lesions and gutter and immune ring of the studied groups

		Bacterial (n=7)	Fungal (n=35)	Mooren (n=2)	neurotrophic ulcer (n=4)	PUK (n=2)	P-value	
Satellite lesions	0 (0%)	27 (77.1%)	0 (0%)	0 (0%)	1 (50%)	<0.001*		
	P1		<0.001*		---		0.222	
	P2				0.067		0.432	
	P3						1.000	
	P4						0.428	
Gutter and immune ring	0 (0%)	15 (42.9%)	0 (0%)	0 (0%)	0 (0%)	0.057		

*: Statistically significant as P value < 0.05, PUK: Peripheral ulcerative keratitis, P1: P values compared to bacterial group, P2: P values compared to fungal group, P3: P values compared to mooren group, P4: P values compared to neurotrophic group.

Table 5: Corneal sensation of the studied groups

		Bacterial (n=7)	Fungal (n=35)	Mooren (n=2)	neurotrophic ulcer (n=4)	PUK (n=2)	P-value
Normal	7 (100%)	31 (88.6%)	2 (100%)	0 (0%)	2 (100%)	<0.001*	
Diminished	0 (0%)	4 (11.4%)	0 (0%)	4 (100%)	0 (0%)		
P1		0.347		---	0.003*		---
P2				0.613	<0.001*		0.612
P3							0.067
P4						0.067	

*: Statistically significant as P value < 0.05, PUK: Peripheral ulcerative keratitis, P1: P values compared to bacterial group, P2: P values compared to fungal group, P3: P values compared to mooren group, P4: P values compared to neurotrophic group.

Case presentation

Case 1

Male patient aged 26 years old with resistant bacterial corneal ulcer.



Fig 1: Male patient aged 26 years old with resistant bacterial corneal ulcer

medical history.

Visual acuity: 6/60.

Corneal ulcer: Ulcer size: 1x1 mm, ulcer site: Peripheral, depth of ulcer: <20%, edge of ulcer: Rounded, Bed of ulcer: Stromal infiltrated, stained with fluorescein, hypopyon: No. and corneal sensation: Diminished.

Culture result: mixed bacterial and fungal

Treatment: Medical treatment

Case 2

Male patient aged 54 years old with resistant bacterial corneal ulcer.

History: Foreign body removal one month ago and negative

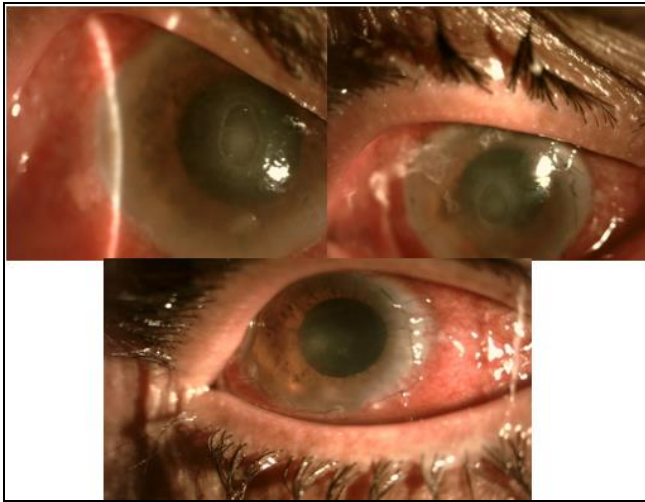


Fig 2: Male patient aged 26 years old with resistant bacterial corneal ulcer

History: Trauma three weeks ago and medical history: Diabetes mellitus five years ago.

Visual acuity: CF50 cm.

Corneal ulcer: Ulcer Size: 2 x1 mm, ulcer site: Central, depth of ulcer: <20%, edge of ulcer: RoundedS, Bed of ulcer: Stromal infiltrated, stained with fluorescein, hypopyon: No. and corneal sensation: Normal.

Culture result: Mixed bacterial and fungal.

Treatment: Medical and surgical treatment.

Discussion

Corneal infections are a significant cause of visual morbidity on a globally, which results in an estimated 2 million cases of unilateral blindness every year and a significant burden on systems of healthcare [4].

In current study, age and gender were insignificantly different among the studied groups. Medical history was substantially different among the studied groups (P value<0.001); DM was higher in fungal keratitis. Age ranged from 26-57 and male was predominant, which might be explained by the fact that they participate in more outdoor activities and are thus more vulnerable to external agents inflicting corneal injury.

Our results are supported by Siang *et al.*, [5] research, which examined the prognostic factors for the visual outcome in microbial keratitis and examined the demographic traits, risk factors, and contemporary trends of the causative organisms. A number of 75 eyes of 74 individuals who were hospitalized at the hospital were evaluated. They demonstrated that the male/female ratio was 13.8:1. The mean age of the patients in this study was 48 years old, and 70% of them were in the productive age range of 20 to 59.

In our study, regarding clinical diagnosis of the studied patients, 7 (14%) patients had bacterial infection, 35 (70%) had fungal infection, 2 (4%) had mooren ulcer, 4 (8%) had neurotrophic ulcer and 2 (4%) had PUK.

In the same line with our findings, Chidambaram *et al.*, [6] found that of 252 patients with severe MK, 18 had AK, 191 had FK, 19 had BK, 4 had mixed BK/FK, and 20 were negative microbiologically.

In this study, 5 (71.4%) patients in bacterial group, 20 (57.1%) patients in fungal group were subjected to trauma. The incidence of trauma was significantly different between

all studied groups (P value=0.040), it was increased in fungal group compared to neurotrophic group (P value = 0.047), while it was insignificant among bacterial, mooren and PUK groups. In our study, 1 (14.3%) patient in bacterial group, 6 (17.1%) patients in fungal group were wearing contacts. Number of patients wearing contacts was insignificantly different among the studied groups. In the current study, 1 (14.3%) patient in bacterial group, 2 (5.7%) patients in fungal group and no patients in mooren, neurotrophic or PUK groups had foreign bodies. The presence of foreign bodies was insignificantly different among the studied groups.

Our results agreed with, Chidambaram *et al.*, [6] who observed trauma in 13 (68%), 134 (70%), 13 (72%), and 17 (85%); p=0.563 in BK, FK, acanthamoeba keratitis and absence of organism respectively.

Similarly, Siang *et al.*, [5] reported that ocular trauma (specifically foreign bodies in the cornea) was the primary risk factor for microbial keratitis.

Our findings reported that ulcer size was insignificantly different among the studied groups. In current study, regarding depth of ulcer, there was a substantial variation between bacterial group in comparison to fungal, mooren, neurotrophic and PUK groups (P value <0.05). There was no substantial variation among fungal, mooren, neurotrophic and PUK groups. In our study, regarding edge of ulcer, there was a substantial variation between bacterial group in comparison to fungal group (P value <0.001), and between fungal group in comparison to mooren, neurotrophic and PUK groups (P value<0.05). In this study, number of participants who had feathery ulcer edge in fungal group was substantial increased more than other groups (P value<0.001).

In their study, Schaefer *et al.*, [7], 3 of the five individuals included in their research who had a poor visual prognosis had ulcers measuring 2 x 2 mm, and the center of the cornea was Vected in 2 of the participants. In all but one instance, the ulcerations were at least 60% of the depth of the whole cornea. The depth of the ulcers seemed to be more important for visual prognosis at that point than the size and location of the ulcer. In the current study, regarding bed of ulcer, there was a significant difference between fungal group in comparison to neurotrophic group (P value<0.001) but there was no significant difference among other groups.

In agreement with our results, Chidambaram *et al.*, [6] reported that stromal infiltrate size was bigger in no organism group followed by fungal and bacterial keratitis. It is explained as stromal infiltrate is a diagnostic feature of resistance keratitis.

Our findings regarding satellite lesions, there was a significant difference between fungal group in comparison to bacterial and neurotrophic groups (P value <0.001 and P value=0.006 respectively) but there was no significant difference between other groups. The incidence of satellite lesions in fungal group was significantly higher than other groups. Gutter and immune ring was insignificantly different among the studied groups.

In agreement with our results, Chidambaram *et al.*, [6] reported that satellite lesions the incidence of satellite lesions in fungal group was substantial increased more than other groups.

In this study, corneal sensation was substantially variant between the studied groups (P <0.001). The incidence of diminished corneal sensation in neurotrophic group was significantly higher than bacterial and fungal groups (P value< 0.05).

In the current study, hypopyon level was insignificantly

different among the studied groups. 15 (42.9%) patients in fungal group and 3 (75%) in neurotrophic group had degree III hyperemia. 19 (54.3%) patients in fungal group, 1 (50%) in mooren group and all patients in PUK group had degree IV hyperemia. Degree of hyperemia was substantially variant between the studied groups (P value <0.05).

Our findings are confirmed by Chidambaram *et al.*,^[6] who stated that hypopyon level was higher in fungal keratitis than other groups.

In this study, regarding culture results of the studied patients, 9 (18%) patients had negative culture, 1 (2%) had bacterial culture and 40 (80%) had mixed (both bacterial and fungal) culture. The cultural positivity rate in this study was 18%, which was less than the research by Otri *et al.*,^[8] in the United Kingdoms (41%), Omar *et al.*,^[9] in Malaysian urban areas (47.5%), and the research by Sand *et al.*,^[10] in the United States (63-82%). This variance may be caused by corneal scraping method, techniques of culture, kinds of pathogenic organisms^[9], various types of culturing media, and antibiotic therapy before corneal scraping^[8]. A positive culture allows for a sensitivity test and enhances the chance to manage the infection, therefore using the suitable culture media, scraping method, and specimen handling might improve the culture outcome^[8, 9].

Conclusion

Clinical diagnosis is more important for treatment and follows up while culture is performed for documentation of the clinical findings. The initial therapy strategy might be guided by evidence of microbiologic trends of infectious keratitis, clinical impressions, and sensitivity/resistance patterns in our area.

Declaration

No Funds, All participants in the research agree to publish

Conflict of Interest

Not available

Financial Support

Not available

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