

The characteristics of clinical, microbiological and antibiotic resistance profile in patients with bacterial keratitis at Ho Chi Minh City Eye Hospital in 2020

Hong-Bao Tran, Hoang-Huy Le*, Dang-An Phan, Thai-Hung Pham, Huu-Loc Nguyen, Thi-Diem-Phuc Tran, Nguyen-Huan Pham

ABSTRACT

Purpose: To investigate the epidemiological, clinical, microbiological characteristics and antibiotic resistance profile in patients with bacterial corneal ulcers at Ho Chi Minh City Eye Hospital in 2020. **Methods:** An observational retrospective study was conducted on 242 cases diagnosed with bacterial corneal ulcers examined at Ho Chi Minh City Eye Hospital from January 2020 to December 2020. Information about patients' medical history, clinical symptoms, and test results was collected from medical records. **Results:** Bacterial keratitis was more often seen in males and in middle-age group. Injury as a risk factor accounted for a considerable proportion of cases (24,4%). Self-treatment was common (23,1%). The culture results were mainly Gram-positive (56,6%), in which coagulase-negative staphylococci (49,2%) predominates. *Pseudomonas aeruginosa* (26,9%) was the most common Gram-negative pathogen. The resistance rate of coagulase-negative staphylococci to common antibiotics, including fluoroquinolones group, was relatively high (50,0 – 100,0%). Meanwhile, *Paeruginosa* was sensitive to many fluoroquinolones, as well as to tobramycin and ceftazidime. Notably, we recorded twelve cases of resistance to all tested antibiotics. The rate of visual acuity improvement at the time of discharge was still unfavorably low (5,8%). There were 43,0% of patients experiencing at least one serious complication: increased intraocular pressure, endophthalmitis, impending perforation and perforation of the cornea. Up to 11,6% of patients had to resort to enucleation. **Conclusions:** Corneal ulceration related to trauma accounted for a significant percentage. Self-medication was still common. The high rate of antibiotic resistance along with the appearance of numerous multi-drug resistance cases is very worrying. Severe consequences were left upon patients' eyesight.

Key words: corneal ulcer, bacterial keratitis, bacteria, antibiotic resistance, Ho Chi Minh city

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INTRODUCTION

Ulcerative keratitis is a commonly seen ophthalmic disease, especially in developing countries. This is a dangerous disease, not only threatens vision but can also cause many complications such as corneal scarring, neovascularization, perforation... The consequence if not treated is usually a partial or complete loss of vision, inflicting long-term sequelae on the patient.

Causative organism may include: bacteria, fungi, viruses, *Acanthamoeba*,... of which, bacteria are often cited as a very prominent agent, leading the number of ulcerative keratitis cases in many regions of the world and second only to fungi in Asia.¹⁻⁴

At the same time, similar to other infectious diseases, the uncontrolled use of antibiotics has caused many cases of antibiotic resistance to first-line antibiotics as well as multidrug resistance to appear, further complicating treatments.

Currently in Vietnam, researches about local patterns of drug resistance, especially more recent ones in ulcerative keratitis, are still scarce. Therefore, we conducted a study to investigate the profile of bacterial drug resistance in ulcerative keratitis patients at Ho Chi Minh City Eye Hospital in the period from January 1, 2020 to December 31, 2020.

MATERIAL – METHODS

Research subjects

All patients diagnosed and treated for bacterial keratitis at the Cornea Department of Ho Chi Minh City Eye Hospital from January 1, 2020 to December 31, 2020. Cases without related identification cultures and antibiograms were not included in the study.

Methodology

Descriptive, retrospective study

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Information collected from the medical record form included the following: administrative informations, onset circumstance, affected eye(s), initial signs and symptoms, time of hospitalization since onset of symptoms, previously used medications, visual acuity at admission, lesion location, size and depth, anterior chamber suppuration, complications, treatment duration, treatment procedures used, culture results for bacterial identification, results of antibiograms and visual acuity at discharged.

RESULTS

Among 242 patients in our study, there were 162 men and 80 women, with the male:female ratio being 2:1. The average age of the patients in the study was 56.4 years old and the majority were of working age.

Regarding onset circumstances, 24.4% of our patients had trauma-related onset of corneal ulcers.

Our research showed that 76.8% of patients had treatment before admission. Among treatment methods, antibiotics were the most reported drug group, used in 14.0% of patients who had previously self-treated. Up to 83.3% of previously treated patients did not know what medicine they used (Figure 1).

Most patients tended to get medical attention early, within 7 days from symptom onset (45.5%). However, up to 22.7% of patients came to hospital more than 28 days after onset of symptoms (Figures 2 and 3).

Concerning visual acuity (VA) at admission, the light perception (LP) to hand motion (HM) group accounted for the highest proportion (67.8%). The rate of hospitalized patients with visual acuity lower than 1/10 at admission was up to 95.0% (Figure 4).

Central and total were two lesion locations with the largest proportion: 50.4% (122 cases) and 30.6% (74 cases) respectively. Lesions more than 6 mm in diameter are commonly seen, with the combined rate of two size groups which can cover the pupil completely, causing vision loss (≥ 6 mm group and 3 - 5 mm group), was up to 93.0%. In cases where the lesion depth was recorded, 42.2% (102 cases) of total cases had lesion greater than 2/3 of the corneal thickness in depth (Table 1). Often accompanied ulcers was purulent discharge in the anterior chamber, with 43.1% of patients having 1 - 3 mm of hypopyon. The > 3 mm group, synonymous with an indication for anterior chamber washout, had a 7.0% rate.

About complications, we noted that corneal perforation was the most regular, accounting for 24.8% (60 cases), followed by impending perforation with a rate of 18.6% (45 cases). Endophthalmitis was the least recorded complication with a rate of 2.9% (7 cases).

Most of our patients (76,9%) were hospitalized for less than 15 days. There were 166 cases that required treatment with at least one medical procedure, accounting for 68.6%. Among them, the most performed treatment procedures are tissue adhesive application, anterior chamber washout, and ocular amniotic membrane transplant with implementation rates of 29.3%, 16.9%, and 15.3%, respectively. Enucleation rate was up to 11.6%.

The proportion of patients discharged from the hospital with visual acuity at NLP was 19.4%. The total rate of patients discharged from the hospital with vision lower than 1/10 is 97.1%. Most patients (83.1%) did not have vision improvement (Figure 4).

According to our data, most ulcerative bacterial keratitis cases were caused by gram-positive bacteria with 137/242 cases (56.6%). The most common gram-positive bacteria were coagulase-negative staphylococci with 113/242 cases, accounting for 49.2%. On the other hand, among gram-negative bacteria, the agent with the highest positive culture rate was *Pseudomonas aeruginosa* with 65/242 cases (26.9%) (Table 2). Furthermore, fungal coinfection was seen in 23.1% of cases of ulcerative bacterial keratitis.

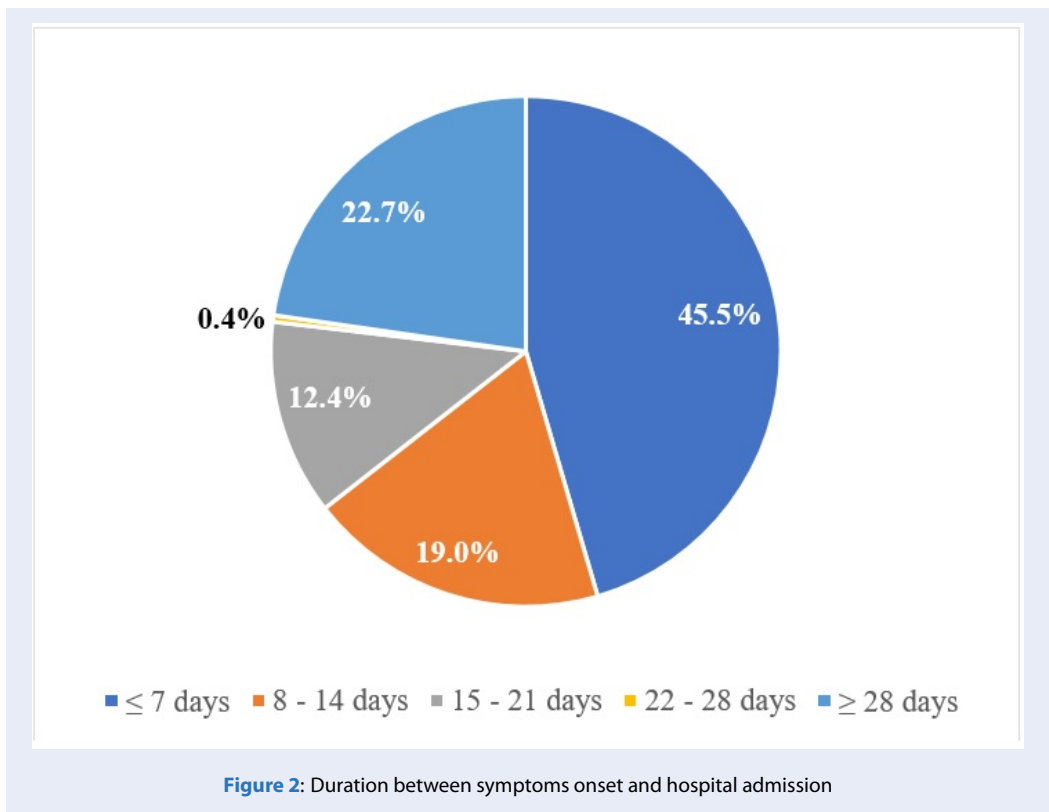
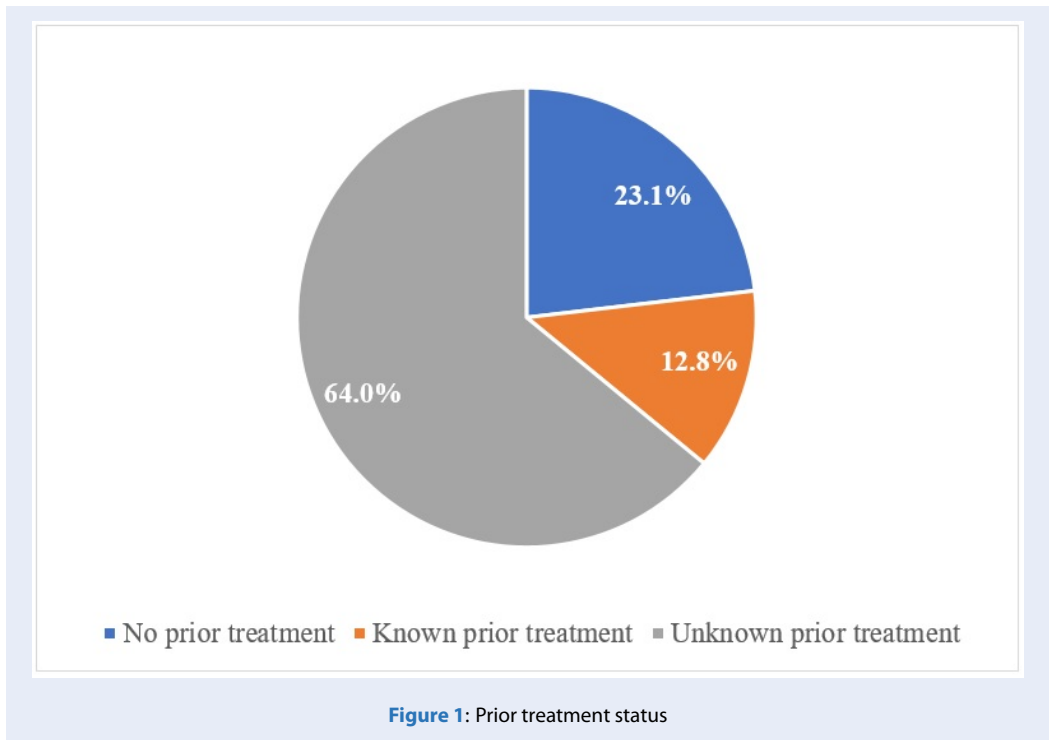
The antibiotic resistance profile of several common bacterial species was also investigated.

In the Gram-positive group, our study recorded high antibiotic resistance rate (50% or more) to all included commonly used antibiotics in coagulase-negative staphylococci, in which the resistance rate to the first-line fluoroquinolone group ranged from 73.1 - 84.9%. Similarly, the resistance rate of streptococci to commonly used antibiotics is often high, with only sensitivity to chloramphenicol group was retained (9.1%).

In the Gram-negative group, *Pseudomonas aeruginosa* was recorded to have a high resistance rates to eomycin (95.2%) and chloramphenicol (100%). Nevertheless, *Paeruginosa* is still sensitive to most fluoroquinolone antibiotics, except moxifloxacin (92.5%) as well as most other antibiotic groups. On the other hand, *Proteus mirabilis* has a high resistance rate to the fluoroquinolone group (71.4 - 87.5%)

DISCUSSION

Our study noted that most of the patients were men and of working age, similar to previous studies in Vietnam and other Asian countries.^{2,5-8} This may be due to outdoor working environment and people's general lack of awareness about using protective glasses. Bacterial keratitis usually only happens on eyes with risk factors, the leading of which in our study was



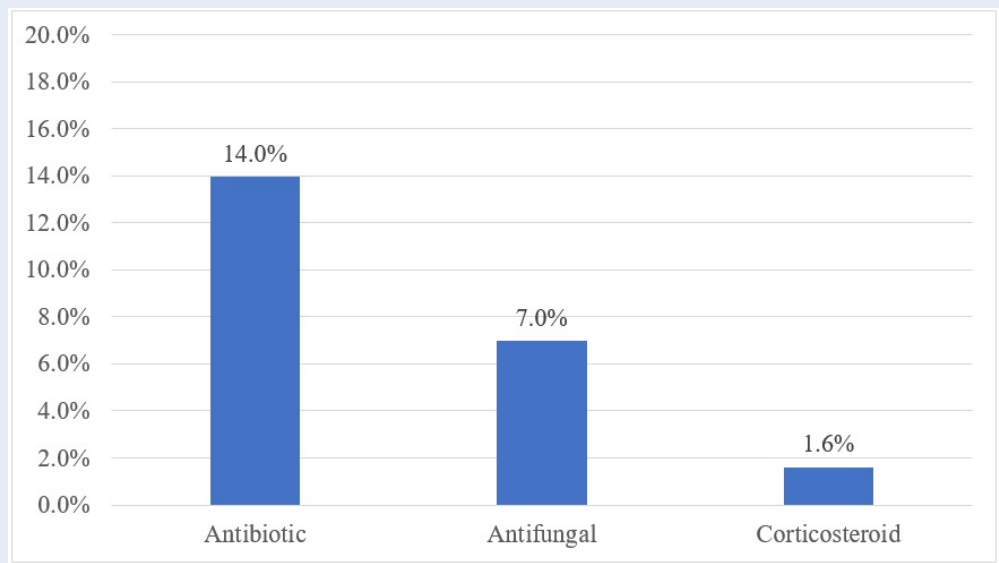


Figure 3: Known medication used before admission

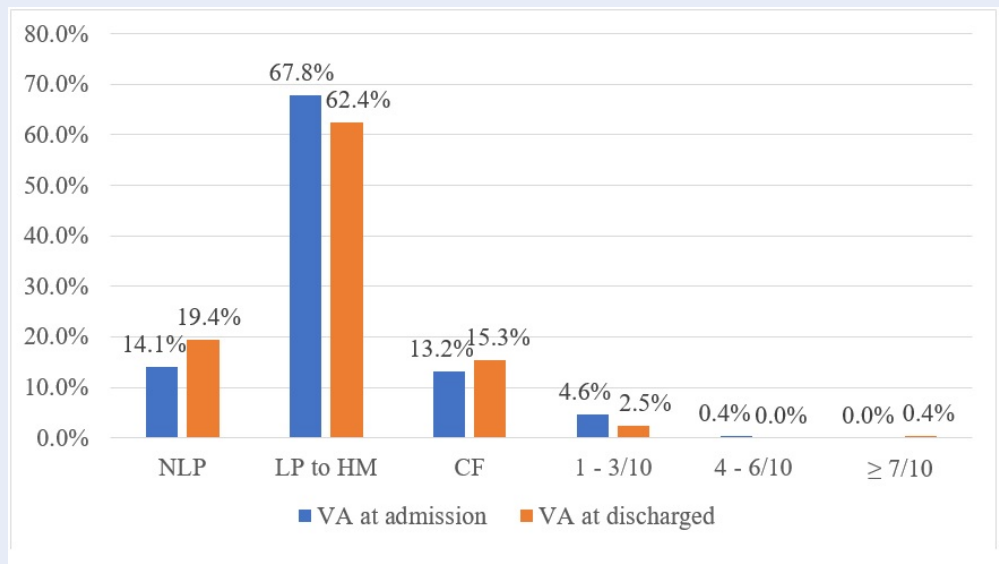


Figure 4: Visual acuity at admission and discharge

traumatic incidents. In developing countries, including Vietnam, the risk of bacterial keratitis related to agricultural injuries or foreign objects is significantly higher.^{2,9}

The majority of our patients come to the hospital within 7 days of symptom onset. Thus, compared to domestic studies from 1998 to 2007, our patients arrived much earlier and equivalent to studies in the recent 5 years.^{6,10-12} Development in socio-economic factors, people’s general knowledge and healthcare

awareness as well as development in transportation had created favorable conditions for people to access specialized hospitals earlier.

On the contrary, up to 76.9% of patients had treatment before hospitalization, with most did not know the medication they were using. Many patients indiscriminately used eye drops without an ophthalmologist’s prescription, especially antibiotics which are the most recorded in research, often leading to patients using eye drops of the wrong type, concentration, and

Table 1: Clinical features

Lesion characteristic	Site	Center	Percentage
		Edge (no pupil involvement)	16.12%
		Distance to center ≥ 3 mm	2.89%
		Total	30.58%
	Size	< 3 mm	7.02%
		3 - 6 mm	40.91%
		≥ 6 mm	52.07%
	Depth	< 1/3 corneal thickness	2.07%
		1/3 - 2/3 corneal thickness	4.13%
		$\geq 2/3$ corneal thickness	42.15%
		Can not be evaluated	13.64%
		Not recorded	38.02%

Table 2: Microbiological profile

		Percentage	Samples
Gram-positive	Staphylococci coagulase (-)	49.17%	119
	Staphylococci coagulase (+)	2.07%	5
	Streptococci	5.37%	13
	Bacilli	2.48%	6
Gram-negative	<i>Pseudomonas aeruginosa</i>	26.86%	65
	<i>Proteus mirabilis</i>	3.31%	8
	<i>Enterobacter</i> spp.	0.83%	2
	<i>Serratia</i> spp.	0.41%	1
Others		9.50%	23

dosage. As a result, the rate of antibiotic resistance is increasing, especially against the fluoroquinolones group.^{13,14}

Regarding clinical characteristics, most patients were hospitalized with severe symptoms: heavily impaired vision (95.0% of patients have vision less than 1/10), corresponding to clinical progression with large and deep lesions located centrally or totally, often accompanied by hypopyon in the anterior chamber. Even when patients are hospitalized early, corneal ulcers are still a serious disease, not only affecting vision but also creating complications: nearly half of the cases had at least one serious complication, in which corneal perforation was the most frequent, happened in up to 1/4 of our cohort. The process of corneal inflammation and ulceration also irreversibly replaces transparent corneal tissue with scar, seriously affecting the patient’s vision. Treatment procedures such as

tissue adhesives application, anterior chamber washing or amniotic membrane transplantation are mostly conservative, limiting the scope of damage done and reducing painful symptoms, with most patients not seeing improvement in visual acuity at the time of discharge. Even with optimal treatment, some patients still ended up having to resort to enucleation.

Regarding microbiological characteristics, bacterial keratitis cases were mainly caused by gram-positive bacteria, with the dominant species being coagulase-negative staphylococci and *Pseudomonas aeruginosa*. Similar to previous domestic studies, our study noted a significantly higher occurrence of gram-negative bacteria in Vietnam compared to other, developed countries, a factor that could influence practitioners’ choice of first-line antibiotic (Table 3).

The study also recorded many cases of bacterial accompanied by fungal infections, consistent with the

Table 3: Commonly recorded causative organisms

Country (Year published)	Author	Gram stain		Most common Gram (+) organism	Most common Gram (-) organism
		Gram (+)	Gram (-)		
U.S (2020)	Asbell	77.50%	22.50%	<i>Staphylococcus aureus</i>	<i>Pseudomonas aeruginosa</i>
Mexico (2015)	Hernandez-Camarena	75.84%	24.16%	<i>Staphylococcus epidermidis</i>	<i>Pseudomonas aeruginosa</i>
Australia (2019)	Cabrera-Aguas	78.03%	21.97%	<i>Staphylococci coagulase (-)</i>	<i>Pseudomonas aeruginosa</i>
Vietnam (2014)	Trần Anh Tuấn	58.00%	42.00%	<i>Staphylococci coagulase (-)</i>	<i>Pseudomonas aeruginosa</i>
Vietnam (2023)	This research	56.61%	43.39%	<i>Staphylococci coagulase (-)</i>	<i>Pseudomonas aeruginosa</i>

climate and agriculture-focused economy of Vietnam. Keratitis caused by co-infection of bacteria and fungi can cause difficulty in initial diagnosis due to overlapping clinical symptoms, leading to increased treatment burden.

In general, when compared with previous foreign and domestic studies, the rate of antibiotic resistance seen in bacterial keratitis patients was at a higher level (Figures 5 and 6).^{5,15-18} Ophthalmic fluoroquinolones that are often used first-line in bacterial keratitis, such as moxifloxacin, show high resistance rates in most bacterial groups surveyed. An increasingly worrying fact is that multidrug resistance occurs frequently, accompanied by the appearance of many cases of resistance to all antibiotics available on the antibiogram.

CONCLUSIONS

In summary, our research has shown a rising trend in resistance rate of commonly seen organisms in bacterial keratitis, such as coagulase-negative staphylococci and *Pseudomonas aeruginosa*. Better education is needed to reduce the indiscriminate use of antibiotics among people, while further multi-center research may be warranted to determine the overall resistance rate domestically, creating the basis for an effective treatment protocol for the region.

LIST OF ABBREVIATION

- VA: Visual acuity
- NLP: No light perception
- LP: Light perception
- CF: Counting fingers
- HM: Hand motion

COMPETING INTERESTS

The authors declare that they have no competing interests.

ETHICS IN RESEARCH

This study has been approved by the Ethics Committee of School of Medicine, VNU-HCM under grant number 03/QĐ-IRB-VN01.017

AUTHORS' CONTRIBUTION

H.H.L, D.A.P, T.H.P, H.L.N and T.D.P.T collected patients' data and wrote the manuscript. H.B.T introduced the study and revised the manuscript. N.H.P operated the study group and makes the final revision.

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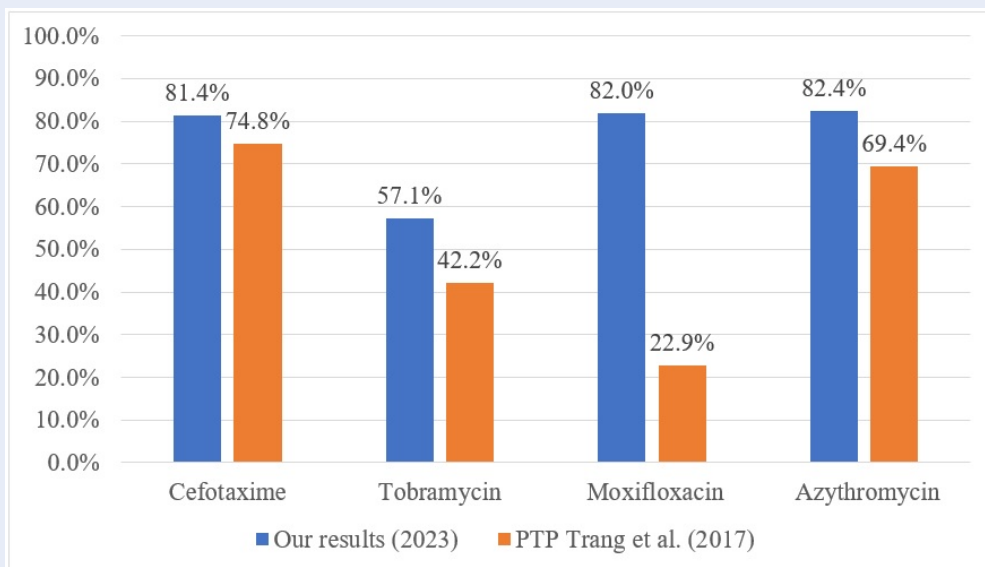


Figure 5: Coagulase-negative staphylococci antibiotic resistance profile

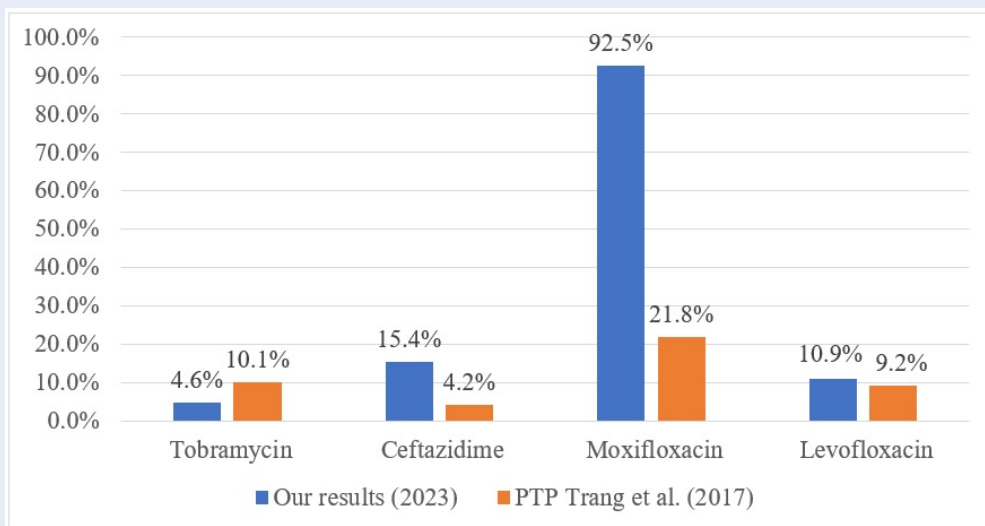


Figure 6: Pseudomonas aeruginosa antibiotic resistance profile

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Khảo sát đặc điểm lâm sàng, vi sinh và đề kháng thuốc kháng sinh trên bệnh nhân viêm loét giác mạc do vi khuẩn tại Bệnh viện Mắt Thành Phố Hồ Chí Minh trong năm 2020

Trần Hồng Bảo, Lê Hoàng Huy*, Phan Đăng An, Phạm Thái Hùng, Nguyễn Hữu Lộc, Trần Thị Diễm Phúc, Phạm Nguyễn Huân

TÓM TẮT

Mục tiêu: Khảo sát đặc điểm dịch tễ, lâm sàng, vi sinh và đề kháng thuốc kháng sinh trên bệnh nhân viêm loét giác mạc do vi khuẩn tại Bệnh viện Mắt Thành phố Hồ Chí Minh trong năm 2020.

Phương pháp nghiên cứu: Nghiên cứu hồi cứu, mô tả thực hiện trên 242 trường hợp được chẩn đoán viêm loét giác mạc do vi khuẩn đến khám tại Bệnh viện Mắt Thành phố Hồ Chí Minh từ 1/2020 đến 12/2020. Các thông tin về tiền sử, bệnh sử, triệu chứng lâm sàng và kết quả xét nghiệm được thu thập từ mẫu hồ sơ bệnh án.

Kết quả: Viêm loét giác mạc do vi khuẩn tập trung ở nam giới (tỷ lệ nam:nữ là 2:1) và độ tuổi trung niên. Yếu tố nguy cơ chấn thương chiếm tỷ lệ đáng kể (24,4%). Tình trạng tự ý điều trị là phổ biến (23,1%). Kết quả nuôi cấy chủ yếu là vi khuẩn Gram dương (56,6%), trong đó staphylococci coagulase âm (49,2%) chiếm ưu thế. *Pseudomonas aeruginosa* (26,9%) là tác nhân Gram âm thường gặp nhất. Tỷ lệ đề kháng của staphylococci coagulase âm với các kháng sinh thông dụng, bao gồm nhóm fluoroquinolones, là tương đối cao (50,0 – 100,0%). Trong khi đó, *Pseudomonas aeruginosa* còn nhạy với nhiều kháng sinh nhóm fluoroquinolones, cũng như với tobramycin và ceftazidime. Đặc biệt ghi nhận 12 trường hợp kháng tất cả các loại kháng sinh trong kháng sinh đồ. Tỷ lệ cải thiện về mặt thị lực tại thời điểm xuất viện còn rất thấp (5,8%). Có 43,0% bệnh nhân gặp ít nhất một biến chứng nặng: tăng nhãn áp, viêm mủ nội nhãn, loét thủng và thủng giác mạc. Có đến 11,6% bệnh nhân phải mổ bỏ mắt.

Kết luận: Viêm loét giác mạc liên quan đến chấn thương chiếm tỷ lệ cao. Tình trạng tự ý điều trị vẫn còn phổ biến. Tỷ lệ kháng kháng sinh hiện ở mức cao với sự xuất hiện của nhiều trường hợp đa kháng kháng sinh là rất đáng quan ngại. Hậu quả để lại cho thị lực người bệnh là nặng nề.

Từ khoá: viêm loét giác mạc, vi khuẩn, kháng kháng sinh, thành phố Hồ Chí Minh

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