

## **Pythium Keratitis: An Underdiagnosed Disease in Bangladesh**

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### **ABSTRACT:**

**Introduction:** *Pythium keratitis* is a newly emerging ocular disease caused by an organism, *Pythium insidiosum* (*P. insidiosum*). It is a sight-threatening disease with high morbidity. **Objective:** To study the clinical features, demographical profile, treatment outcome, and ocular morbidity of microbiologically proven pythium keratitis. **Methods:** This retrospective study, reviewed the medical case records of patients of *Pythium keratitis* attended at indoors and out-patient department in LV Prasad Eye Institute, Hyderabad, India, from January 2017 to October 2019. For the purpose of this study, only microbiologically confirmed either with Potassium Hydroxide (KOH) smear or culture positive cases were included. **Results and Conclusion:** The study was conducted on 153 cases, 62 males and 91 females. It comprises 6.4% of total keratitis reported within this period. Unlike fungal keratitis vegetative matter injury plays a minor role in this case. *Pythium keratitis* is more prone to develop in agriculture workers. The outbreak of pythium keratitis was more in rainy season peak in the month of June- October. Initial presentation was with typical features of Tentacles (56%), Dots like infiltrate (47%), Plaque like lesions (17%), Ring infiltrate (22%), Peripheral guttering (53%), Endo-exudates (37%), Hypopyon was present in almost all the cases. Most of the cases were treated with antifungals and antibiotics before final diagnosis. Evisceration, loss of sight, and therapeutic penetrating keratoplasty rate were significantly reduced with the advent of medical treatment. Linezolid and Azithromycin showed greater zone of inhibition. An increase in awareness among the microbiologist and ophthalmologist is very important to manage pythium keratitis.

**Key Words:** *Pythium keratitis*, Tentacles, Linezolid.

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### **INTRODUCTION:**

*Pythium keratitis* is an uncommon but sight-threatening disease with high morbidity. It occurs when the cornea is infected by *Pythium insidiosum* (*P. insidiosum*). *P. insidiosum*, belonging to the kingdom Stramenopila, is a fungus like, aquatic

oomycete found in tropical, subtropical, and temperate climates.<sup>1-4</sup> It was long misdiagnosed as a fungus due to its fungus-like morphologic characteristics. It also causes life threatening infection in human and animals.

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Majority of the reports have so far been primarily from Thailand.<sup>5</sup> In recent years many cases of *P. insidiosum* keratitis have been reported in several countries, including Thailand,<sup>5</sup> India,<sup>6,7</sup> Australia,<sup>8</sup> Haiti,<sup>9</sup> New Zealand,<sup>10</sup> Israel,<sup>11</sup> Malaysia.<sup>12</sup> Canada,<sup>13</sup> France,<sup>14</sup> Spain,<sup>15</sup> and China.<sup>16</sup> The most challenge in management is its diagnosis. It is almost always misdiagnosed as fungal keratitis. In KOH wet film preparation it morphologically resembles that of fungus. It has no ergosterol in the cell membrane and lack of chitin and cellulose in the cell wall. Thus it does not response on antifungal medication and looks folded ribbon like non septate filaments under the microscope.<sup>17,18</sup>

In Bangladesh pythium keratitis is less discussed disease. Due to insufficient knowledge among the medical and laboratory personnel the disease is misdiagnosed as fungal keratitis.

Pythium keratitis shows hyphate edges of the infiltrates resembles tentacles like lesion, dot like infiltrate at the mid stromal level surrounding the main infiltrate, peripheral gutter and hypopyon.<sup>7,19</sup>

Microscopic examination with 10% KOH wet mount preparation shows ribbon like folded aseptate filaments. Culture shows colorless or light brown color on blood agar plate of pythium species. The culture may further processed for identification of

zoospores formation. DNA extract, PCR, DNA sequencing are the confirmatory diagnosis.<sup>19</sup>

Effective treatment strategy has not yet to be developed. Study shows Linezolid, Azithromycin, Tetracycline, Macrolids are sensitive to pythium insidiosum.<sup>20</sup>

In clinical practice large number of fungal keratitis treated with antifungal medications, are not responding. Pythium insidiosum might have been the causative factor some of these non-responding keratitis. Awareness among the ophthalmologist and microbiologist about pythium keratitis is an urgent need in our country.

#### **METHODS AND MATERIALS:**

This retrospective study was carried out in LV Prasad Eye Institute, Hyderabad, India, from January 2017 to October 2019. Retrospectively 153 cases of microbiologically diagnosed pythium keratitis treated in LV Prasad Eye Institute were included.

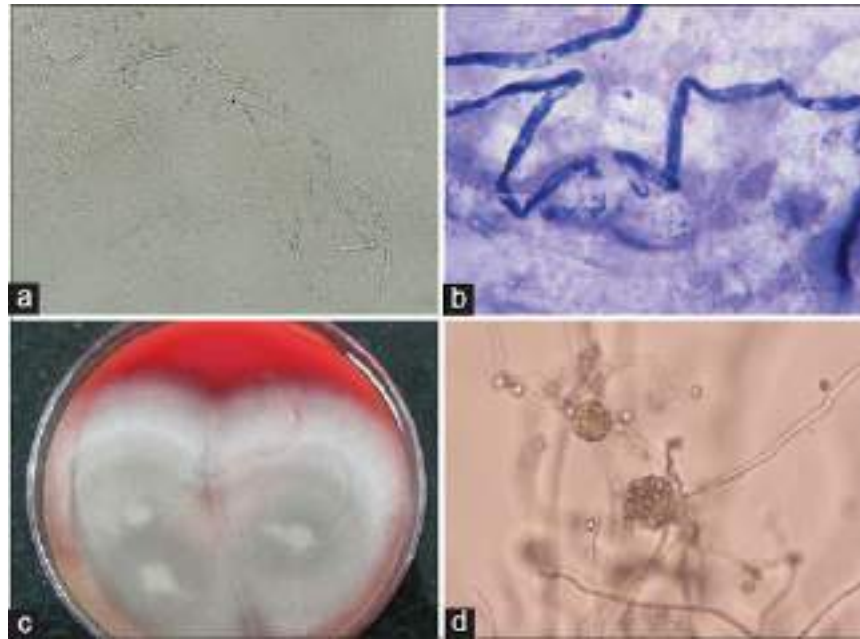
Data was analyzed and processed as frequency and percentage in tables using Micro-Soft Excel statistical program & IBM SPSS (Statistical Package for Social Sciences) program (Version-20).



**Figure 1: A typical presentation of pythium keratitis**



**Figure-2: Clinical findings of a case of pythium keratitis, (a) Central dense, grayish-white infiltrates with Tentacles like lesions, (b) Diffuse Dot-like infiltrates, Peripheral guttering inferiorly, (c) Large dense infiltrates with guttering from 2 o'clock to 7 o'clock position with Hypopyon, (d) Guttering, tentacles –like extensions and subepithelial dot-like infiltrates.**



**Figure 3: (a) Long sparsely septate hyaline hyphae of *Pythium insidiosum* on 10% KOH wet film preparation of corneal scraping, (b) Gram stain image showed the thick cell wall, a few septate, and mass of vesicles inside, (c) A 3 days old culture of *P. insidiosum* at 37°C grown on 5% sheep blood agar. (d) Avesicles with zoospores that developed after 3 h incubation before zoospore release (x10)**

**RESULTS:**

This retrospective study was conducted on 153 microbiologically proven pythium keratitis. In this study females (n-91/59%) were more than males (n-62/41%). The mean age of the patients at presentation was 48±18.2 years (Range: 4–80 years). Among the similar lesions in the eye treated in this period of time, pythium keratitis was 6.4%, where fungal keratitis was 69.3%. More than two third of the patients were presented to other ophthalmologist within one week of onset of symptoms. In this hospital the average reporting time was about 13 days. In most of the cases (64.7%) no causative factors were identified. Some cases Vegetative matter injury (13.1%), Dust particles (7.1%), Injury by nails (4.6%), Insect bites (4.6%), Dirty water exposure (3.3%) and Contact lens user (2.6%) were found.

During the first presentation in this hospital nearly two third (68%) of the patients were reported with visual acuity of counting finger or worst, while (20%) were reported better than 6/60. Patients reported

early with better visual acuity showed better prognosis. Before the final diagnosis almost all the cases were treated with antifungal and antibiotics medications.

Among the 153 patients Diabetes Mellitus was found in 10 cases and 5 cases were also suffering from bacterial infection.

After the diagnosis confirmed, all patients were treated with E/D Linezolid, E/D Azithromycin, E/D Atropine.

**Table 1: Visual Acuity on Reporting:**

Visual Acuity	Number of cases
PLPR	3
CF - HM	104
6/60 to 1/60	26
6/18 to 6/60	12
6/6 to 6/18	8

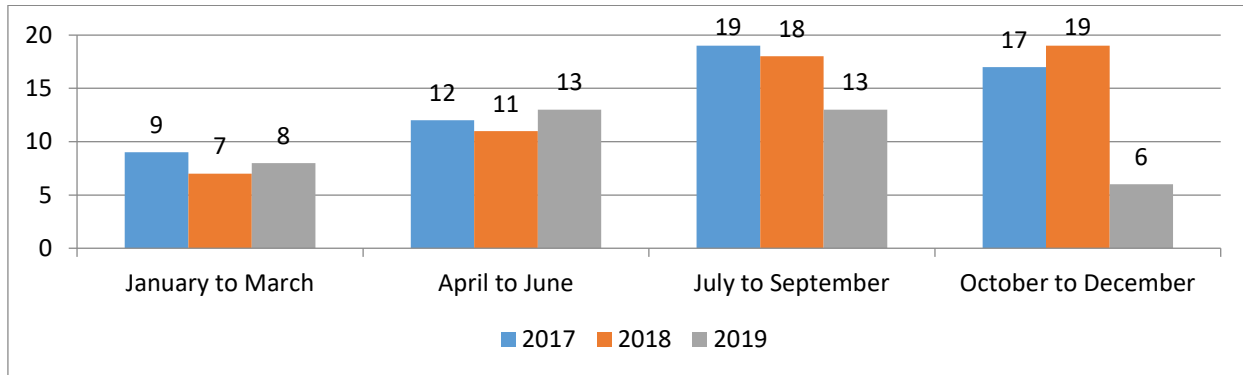
Most of the patients were related to Agriculture (41.1%) and Household works (37.3%). Initial presentation was with typical features of Tentacles

other features were also noted as shown in the table 2.

**Table 2: Clinical Presentation of Pythium Keratitis**

Clinical Signs	Found in Number of Cases
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Tentacles	80
Dots like infiltrate	73
Plaque like lesions	28
Ring infiltrate	32
Peripheral guttering	77
Endoexudates	47
Hypopyon	140



**Figure 1: Seasonal Variation**

Microbiological examination of corneal scraping was done in every patient. In 10% KOH wet mount preparation typical ribbon like folded filaments were

Year	Total Patients	Th PKP	Final VA better than 6/18	Evisceration
2017	58	30	21	5
2018	55	24	25	3
2019	40	15	21	1

found in all cases. Flat feathery colorless colony was found in culture. Linezolid (35 mm) showed greater antibiotic zone of inhibition after 48 hours of culture. Azithromycin (25 mm), Clarithromycin (22 mm), Tetracycline (23 mm), Doxycycline (27 mm), Minocycline (34 mm) also shows significant antibiotic zone of inhibition.

In the year of 2017 out of 58 patients, 30 (51.72%) cases underwent Therapeutic penetrating keratoplasty (Th PK). Final VA more than 6/18 were in 21 (36.20%) cases. In 2018 and 2019 Therapeutic penetrating keratoplasty rate was reduced and visual prognosis was better.

**Table 3: Year-wise analysis of treatment outcome in patients with Pythium keratitis.**

**DISCUSSION:**

*P. insidiosum* keratitis is an emerging highly morbid disease causing vision loss in patients and accounts for 5.9% of cases of Keratitis in South Indian population. The disease has been increasing over the recent years.<sup>6, 21</sup> The mean age of the patients was  $48 \pm 18.2$  years. Bagga, et al showed male predominant but in our study it showed female predominant (59%).<sup>19</sup> Agriculture workers were more prone to develop the disease. The predisposing factor was unknown in many cases. Exposure to foreign body, history of expose to dirty water & other aquatic environments & soil is very imperative to raise the suspicion of *P. insidiosum*. An outbreak of pythium keratitis is more in rainy season reported by Bagga, Hasika & N Permpalung.<sup>7, 19</sup>

Many studies reported its association with water.<sup>14,22</sup> In our study we also found that pythium

keratitis was associated with history of exposure of water and other aquatic environment such as agricultural fields.

The most common clinical characteristic of the corneal lesions were tentacles, dot like infiltrates, peripheral furrowing, endoexudates, hypopyon. All the studies showed these typical presentations of pythium keratitis.<sup>6,7,19,21</sup> Microbiology results of direct microscopy with 10% KOH wet mount preparation showed filamentous fungus (ribbon like folded aseptate filaments). Gram stain was positive in all cases. In the laboratory, colony morphology along with zoospore formation as well as molecular tools helps in the confirmation of the disease. This organism grows rapidly on common laboratory medium.<sup>22</sup>

Permpalung et al showed in Thailand during 2010 to 2016, 14 (47%) patients out of 30 pythium keratitis needs evisceration/ enucleation. In previous studies the rate of globe salvage group were significantly lower (12.5%).<sup>23</sup> Even Though the globe salvage rate has improved from the previous studies from Thailand, it seems to us that ocular surgeries remain the mainstay of treatment in all reports. In the largest study of *P. insidiosum* keratitis from India, showed that the treatment with topical linezolid, topical and systemic azithromycin were added into the treatment regimen in 2016, significantly improved the visual prognosis. They showed none of the case underwent evisceration out of 32 patients.<sup>19</sup>

As pythium is not a fungus and the morphology is different from fungus, antifungal agents are not effective. In vitro activity of antibiotics Linezolid showed highest (31±5 mm) zone of inhibition. In the recent study by Muralidhar et al and in our study, it showed that, patients treated with Linezolid and Azithromycin eye drops were responding well.<sup>17</sup> Earlier, the recurrence was very high even in initial therapeutic penetrating keratoplasty (Th PK) & 91% required evisceration as reported by Krajayven et al.<sup>24</sup> Bagga et al showed Th PK was required in 64% case. All eyes with infiltrates larger than 8 mm required Th PK, indicating that larger ulcers do not respond to medical therapy.<sup>19, 24</sup>

In recent study the role of Th PK improve the visual prognosis significantly. Shweta et.al and earlier reports showed the outcome of surgical management was the mainstay of treatment for pythium keratitis. Cryotherapy was used in patients where pythium was confirmed and infiltrate reached the limbus. Medical treatment with Azithromycin and Linezolid showed favorable clinical outcome in all studies.

## CONCLUSION:

Pythium Keratitis is a sight threatening disease. Early detection & proper treatment can save the vision. In our country the disease also exists but misdiagnosed as fungal Keratitis. There is an urgent need of trained healthcare provides. An increase in awareness among the microbiologist and ophthalmologist is very much essential.

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