Message of the President

Dear Friends

Greetings and wishing you all a very happy 2023. I hope the new year brings happiness and joy to all of you.

Thank fully the covid panic is now faded and hopefully the new strains will also be mild and restricted to mild respiratory infections. It has affected the regular academic programs being conducted and now hopefully we are back on track as we reach nearer to the ISMM conference 2023.

I hope all of you are gearing up for the ISMM conference to be held in Manipur, Imphal under the leadership of Dr. Ranjana. This conference was due in 2021 after the successful conduct of the ISMM conference in Jodhpur. Due to Covid and other factors this biennial conference got postponed to 2023.

Imphal nested in the far east of India is beautiful with the natural beauty worth a place to visit. I hope all the members have registered for the conference and will be presenting their scientific work. The young members should utilize this opportunity to come, meet others and develop scientific collborations. I request all of you to encourage your fellow colleagues to become member of this National body.

The ISHAM congress held in Delhi in October 2022 was grand and fruitful under the leadership of Dr. Arunaloke Chakrabarti and team. We congratulate him once again for organizing this event after a long wait due to the Pandemic.

As far as the upcoming events are concerned I am happy to inform you that we at Sri Ramachandra Medical College will be conducting our Annual workshop in the month of September this year after the online workshop conducted in last two years sometime in the second or third week, final dates will be announced soon.

The first announcement of the TIMM (Trends in Medical Mycology) conference to be held in Athens, Greece has been made. It will be from 20th to 23rd October 2023.

Wishing you a very happy and successful new year once again.

Dr. Anupma Jyoti Kindo
President, Indian Society of Medical Mycologists

Report of General Secretary

It is indeed wonderful to be writing to you all once again.

At the outset wishing you all and your dear ones a year filled with happiness and health.

I am presenting a brief report of what we planned and accomplished in the last year. The committee has met online almost every 2 months to ensure the activities of ISMM have gone on without a hitch.

The fulcrum - Dr. Chakrabarti
Key mycology related activities across the country is spearheaded by Sir. The following require special mention -

- Even during the midst of covid be it the 2nd or the 3rd wave we were able to complete three important covid related mucormycosis multicentre studies. Two were case control and one on environment surveillance and its role.

- To meet the growing need for better management of patients with not just invasive mycosis but others of national importance, ICMR has initiated the process of recognizing referral centres across India to meet this demand. Thus far, centres recognised include - AIIMS Bhopal, AIIMS New Delhi, AIIMS Bhubneshwar, PD Hinduja Mumbai, SJMCH Bangalore, NIMS Hyderabad, KGMU Lucknow, AMC Guwahati with PGIMER coordinating all QC and training activities.

- One of the greatest success stories was hosting the ISHAM 2022 at New Delhi. The committed team of organizing committee was able to ensure smooth and seamless conduct of the entire event.

Academic commitments
- Dr. Anupma and her troop have been undeterred by the challenges of Covid. They continued to have all their mycology workshops. The team from PGIMER with Drs. Shivpakash and Anup Ghosh have been conducting workshops across the nation and now they are targeting training at the tier 2 and 3 centres. Members of ISMM council have been participating as resource faculty in the workshops and CMEs conducted by various centres.

- PGIMER is committed to ensure quality mycology diagnostic services offered by all centres. The EQMM program conducted by them is challenging and is a good teaching material for all students and faculty. I encourage teaching and non-teaching institutions offering mycology diagnostics to enrol in this PT program.

Biennial conference at Manipur

The council has extended all support to Dr. Ranjana to conduct this much-awaited event. It promises to be a great academic feast. Requesting students and young faculty to make the oral and poster presentations highly competitive. The awards are up for grabs. Make the best use. Looking forward to great participation. Please log into the website for the latest updates.

Membership
We have grown in numbers - almost 500 in all now. To make the process of registration easy we are creating a payment gateway which will ensure a quick communication regarding the membership number. This should be completed by end of February. I request the regional council members to motivate young microbiologists in their respective regions to become members of ISMM.

Council
The council has approved the new Regional council member nomination and consent form for circulation. This has been circulated by mail to all members. Request young mycologists to join the council and propel the body to higher levels. The next executive council will be announced in the forthcoming biennial conference GB meeting.

Lifetime achievement award –

I request members to send in nominations of senior eminent mycologists for this prestigious award.

Gratitude

I wish to place on record my sincere gratitude to the entire council headed by Dr. Anupma for their unstinted support and confidence in me to execute my responsibilities. The newsletter is possible only because of Dr. Savitri and I am really indebted to her.

As I sign off as the general secretary of ISMM, my humble request to all of you is - let's make a difference to patient management in our country.

Wishing the new committee the best for years ahead and assurance of all my support.

Thank you and God bless.

Jayanthi Savio
General Secretary, SIHAM

1. Dr. M. J. Thirumalachar Life Time Achievement Award.

TThe Life Time Achievement award is established to honor members of the Society, who during the span of his/her life-time have demonstrated a longstanding commitment to the cause of Medical Mycology in India. The award is made possible by a generous donation by one of the senior most and revered member of the Society, Dr. Arvind A. Padhye,

The award would recognize the significant contribution to the understanding and application of the knowledge pertaining to the Medical Mycology in India, over the entire course of his /her life time, with a definable body of work through one or more of the following:-

- Teaching /Training.
- Research.
- Publications/patents.
- Patient care.

Who may receive the award?

The nominee should be a Life member of the Society in good standing, He should be in the field for at least 25 years but not necessarily active professionally at the time of receiving the award.

He must be alive at the time the selection committee's choice is announced. In case of an unfortunate event of death of the awardee after selection, the award may be presented posthumously.

How will the recipients be chosen?

The president, with the approval of the executive committee, will appoint a Life Time Achievement Awards committee consisting of five active members of the Society. One committee member shall be a current member of the SIHAM executive council, who would co-ordinate the committee meeting. The committee will invite nominations from the members for the award. The nomination is to be made by at least two life members of the society at least 6 months in advance to the next annual conference of the society. Self-Nomination will not be accepted.

The nominations will be scrutinized by the award committee and the best among the nominations will be selected for the award.

When will the award be presented?

The award may be presented to the deserving individual at the Annual Conference of the Society. The awardee will be introduced to the august gathering duly stating his/her achievements during the inaugural function of the Conference.

The award will consist of a citation and a memento.

No travelling or daily allowance will be provided to the awardee to attend the function.

The decision of the award committee will be final.

2. G. P. Agarwal young scientist Award

The best paper award will be given to a young scientist below the age of 35 years (proof of age to be submitted). Applicant must submit the full length original research paper on any area of the medical mycology. Oral presentation of the research should be done in the separate award session during the conference.

3. Dr. Pankajalakshmi Venugopal Glaxo Meritorious Award

Age limit -35 years (proof of age to be submitted). Must submit the curriculum vitae with list of publications and reprints of the papers in the field of medical mycology. Award will be given on the basis of the CV for the outstanding work in the field of medical mycology

4. Dr Kamalam Glaxo award

Applicant must submit full length research paper in duplicate in the field of dermatomycology. Award will be given based on oral presentation in the separate session during the conference.

Minutes of the virtual meeting of the executive council held on the 9th of Jan 2023 Time: 5.00 – 6.00pm

Agenda:

1. ISMM conference
2. ISMM awards
3. ISMM council elections
4. ISMM Newsletter
5. Any other issues as proposed by the members present for the meeting / shared on the group prior to the meeting

Members Present:

1. Dr. Anupma J. Kindo – President
2. Dr. Jayanthi Savio – General Secretary
3. Dr. Anup Ghosh – Treasurer
4. Dr. Savitri Sharma – Editor Newsletter
5. Dr. Pratibha kale – Member [North Zone]
6. Dr. Vinay Kumar Hallur – Member [East Zone]
7. Dr. Shivprakash Rurdamurthi- Special invitee
8. Dr. Ranjana Khuraijam, Organising Secretary, ISMM-Imphal

1. ISMM conference:

Academic Program and awards

- Dr. RK informed the members that the academic program of the conference was almost finalized with help from Drs. AC and SR and that she would share the same with all members as well as it would be communicated on the website.
- Members confirmed that presentations both oral and poster must be open to only members of ISMM.
- A maximum of 3 best papers to be selected in each award category requiring oral presentations.
- To create a checklist document for judges assessing the oral as well as poster presentations for uniform evaluation.
- One award for quiz winner.
- Dr. SR recommended that at least 20 Travel awards must be given at Rs. 5000/- each.

Status of financial support

Dr. RK confirmed that she had received the support from ECMM, ISHAM and she was expecting to receive from other sponsors.

Support for resource faculty

Dr. RK confirmed that she will be supporting the local hospitality to all resource faculty and in addition local travel for international faculty.

2. ISMM Newsletter:

Dr. SS informed that it is getting ready and should be ready for circulation by month end.

3. Lifetime achievement award:

- Dr. JS requested for formats for the awards - plaque and the medal from the PGI team.
- An amount of Rs.10,000/- was decided to get them done. It could be finalized depending on the final quote from the vendors.

4. Council elections:

a. Communication from Dr. Anuradha (zonal member West): Dr. JS informed the members that Dr. Anuradha had communicated her inability to continue in this position as she had moved to another location. It was decided to co-opt Dr. Vijayalatha Rastoghi to represent this region till such time the nominations are received by the council and decisions can be made. Dr. VR to be informed of the same by Dr. JS.

b. The meeting concluded requesting Dr. SS to share the number of nominations received for regional members so that further process could be decided in the next meeting which could probably be the last meeting before the conference.

Answer for the last issue's identify the fungus (ISMM mycoses, Issue 23, Quiz December 2021)

A 55-year-old man presented with fever, progressive breathlessness of three days duration. He was a known type 2 diabetes mellitus case on irregular treatment with oral hypoglycaemic drugs and infrequent blood sugar monitoring. His random plasma glucose at admission was 180 mg/dL. Physical examination revealed bilateral crepts at the lung bases and computed tomography (CT) scan of the chest showed multiple patchy ground-glass opacities in both lungs involving both upper lobes, the right middle lobe, and the lingual lobe. The nasopharyngeal swab was positive for SARS-CoV-2 by RT–PCR. He was started on intravenous dexamethasone. On day 8, bilateral lid edema with right eye prominence was noted and an MRI of the brain, orbits, and paranasal sinuses revealed a soft tissue swelling in the right preseptal, premaxillary, and retrobulbar regions. Sinusitis in the form of significant mucosal thickening in the right frontal, maxillary, and ethmoidal sinus was also seen. Nasal biopsy from the middle turbinate was subjected to microbiological evaluation which included 10% potassium hydroxide (KOH) smear and culture on Sabouraud dextrose agar (SDA). KOH mount showed ribbon like, aseptate hyphae. SDA culture at 25°C on day 3 showed cottony, buff coloured growth which filled the tube. Microscopic findings revealed sporangiophores up to 400 μm high and 10 μm wide, produced in pairs (may be in groups of 1-4). Sporangia were greyish-black, spherical, up to 100 μm in diameter. Columellae were subglobose to globose to conical comprising 80% of the sporangium. Sporangiospores were ellipsoidal or subglobose, up to 5-9 μm in length.

Answer: Correct identification- *Rhizomucor microsporus,* not reported by any one

**Last quiz lactophenol cotton blue mount picture**

Quiz: Can you identify the fungus?

A 38-year-old male presented with the complaints of painless, swelling over the wrist of right hand, gradually increasing in size for 6 months. The patient had a history of diabetes mellitus and underwent renal transplant 3 years back and was on immunosuppressants. He did not recall any history of trauma. The local examination revealed a non-tender, 4 × 4 cm cystic swelling over the dorsum of the wrist. Fine needle aspiration from the lesion was performed and the aspirate was subjected to microbiological evaluation which included 10% potassium hydroxide (KOH) smear and culture on Sabouraud dextrose agar (SDA) at 25°C and 37°C. The KOH mount showed dark septate hyphae and the culture grew cream coloured velvety colonies which turned greyish brown in colour after further incubation (Fig A). The lactophenol cotton blue (LCB) mount from culture is shown in figure B. Please identify the fungus to species level.

Figure A   Figure B
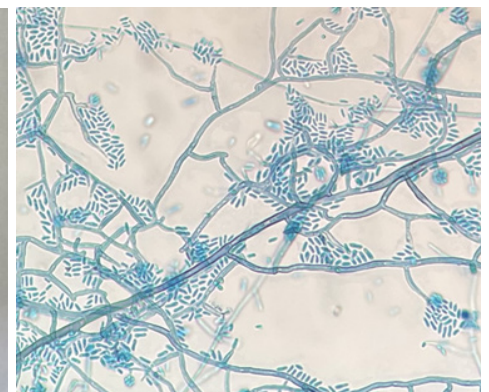
Send your answer to Dr Harsimran Kaur at drharsimranpgi@gmail.com

Results of ISMM Mycology External Quality Assurance Program conducted at PGIMER, Chandigarh

Performance Report of the Participants (25th Batch, July 2021)*

Total number of participating laboratories -131

S No.	Sample/ Code	Clinical details			Correct identification	Interpretation	Laboratory(%) given correct results
		Age/Sex	Clinical feature/ Diagnosis	Source of specimen			
1	EQMM-1	65 yrs/F	COVID+ve, diabetes mellitus, rhino-orbital swelling	Orbital tissue	*Cunninghamella bertholletiae*	Rhino-orbital Mucormycosis	88%
2	EQMM-2	38 yrs/M	Keratitis	Corneal scraping	*Fusarium dimerum*	Fungal keratitis	68.09%
3	EQMM-3	45 yrs/M	Subcutaneous nodular lesion	Skin biopsy	*Exophiala jeanselmei*	Phaeohyphomy-cosis/ Chromo-blastomycosis	33.88%
4	EQMM-4	50 yrs/M	Peritoneal dialysis for peritonitis	Peritoneal fluid	*Paecilomyces variotii*	Fungal peritonitis	64.8%
5	EQMM-5*	28 yrs/M	Meningitis	CSF	*Cryptococcus gatti*	Cryptococcal meningitis	80.57%

Results of antifungal susceptibility testing (AFST) performed for EQMM -5; Laboratories participating in AFST –73. 28%

(EQMM-5) Minimum inhibitory concentration	Ampho tericin B 0.5mg/L	Flucona zole 2.0mg/L	Vorico nazole 0.06mg/L	Itraco nazole 0.5mg/L	Posa Conazole 0.25mg/L	Caspo fungin 0.125mg/L	Anidula fungin 0.25mg/L	Mica fungin 0.3mg/L
Participants results %	96.06%	86.20%	80.45%	18.06%	70.20%	12.06%	19.23%	71.06%

- **Could not be included in 23rd issue of the ISMM Newsletter**

Performance Report of the Participants (26th Batch, Jan 2022)

Total number of participating laboratories -128

S No.	Sample/ Code	Clinical details			Correct identification	Interpretation	Laboratory(%) given correct results
		Age/Sex	Clinical feature/ Diagnosis	Source of specimen			
1	EQMM-1	60 yrs/F	Diabetes mellitus, rhino-orbital swelling	Nasal scraping	*Rhizopus arrhizus*	Rhino-orbital mucormycosis	93.5%
2	EQMM-2	25 yrs/M	Parietal lobe-abscess with seizures	Pus from brain abscess	*Aspergillus flavus*	Fungal brain abscess	97.8%
3	EQMM-3	40 yrs/M	Cutaneous itchy lesion	Skin scraping	*Trichophyton mentagrophytes*	Dermatophytosis	90%
4	EQMM-4	45 yrs/M	Keratitis	Corneal scraping	*Curvularia lunata*	Fungal keratitis	88.4%
5	EQMM-5*	65 yrs/M	Sepsis	Blood culture	*Candida glabrata*	Candidemia	89.9%

Results of antifungal susceptibility testing performed for EQMM -5; Laboratories participating in AFST: 78 .12%

(EQMM-5) Minimum inhibitory concentration	Amphoteri-cin B 0.5mg/L	Fluco-nazole 2.0mg/L	Vorico nazole 0.06mg/L	Itracon-azole 0.5mg/L	Posacon-azole 0.25mg/L	Caspo-fungin 0125mg/L	Anidula-fungin 0.25mg/L	Micafungin 0.3mg/L
Participant results %	89%	93%	88%	21%	10%	91.%	15%	81%

Performance Report of the Participants (27th Batch, July 2022)

Total number of participating laboratories -124

| S No. | Sample/ Code | Clinical details | | | Correct identification | Interpretation | Laboratory(%) given correct results |
		Age/Sex	Clinical feature/ Diagnosis	Source of specimen			
1	EQMM-1	32 yrs/F	Itchy, scaly lesion on skin	Skin scraping	*Microsporum canis*	Dermatophytosis	92.8%
2	EQMM-2	75 yrs/M	Keratitis	Corneal scraping	*Purpureocillium lilacinum*	Fungal keratitis	98.2%
3	EQMM-3	48 yrs/M	Nodular lesion on leg	Skin scraping	*Fonsecaea monophora*	Subcutaneous fungal infection	68.8%
4	EQMM-4	50 yrs/M	Acute myeloid leukaemia, fever, haemoptysis, cough	Bronchoalveolar lavage	*Rhizopus homothallicus*	Pulmonary mucormycosis	89.4%
5	EQMM-5*	78 yrs/M	Sepsis	Blood culture	*Candida albicans*	Candidemia	98.6%

Results of antifungal susceptibility testing performed for EQMM -5; Laboratories participating in AFST: 93.54 %

(EQMM-5) Minimum inhibitory concentration	Amphotericin B 0.5mg/L	Fluconazole 0.12mg/L	Voriconazole 0.03mg/L	Itraconazole 0.03mg/L	Caspofungin 0.03mg/L	Anidulafungin 0.03mg/L	Micafungin 0.03mg/L
Participants results %	83.06%	89.51%	81.45%	11.29%	78.20%	9.67%	70.16%

Abstracts (January – December 2022)

Compiled by Dr. Joveeta Joseph

Microbiologist, Jhaveri Microbiology Centre, L V Prasad Eye Institute, Hyderabad

1. **Epidemiology of Invasive Fungal Infections in Solid Organ Transplant Recipients: an Indian Perspective**

Megha Sharma[1], Shivaprakash M Rudramurthy[2], Arunaloke Chakrabarti[3]

[1]Department of Microbiology, All India Institute of Medical Sciences, Bilaspur, India, [2]Department of Medical Microbiology, Postgraduate Institute of Medical Education and Research, Chandigarh, India, [3]Doodhdhari Burfani Hospital and Research Institute, Haridwar, India

Abstract

Purpose of review: This review summarizes the available Indian data on epidemiology of invasive fungal infections (IFI) in recipients of solid organ transplants (SOT). The epidemiology is further compared with studies from other parts of the world for each SOT type.

Recent findings: The available studies on Indian epidemiology of IFI in SOT are scarce, though the number of SOTs performed in India have increased tremendously in recent years. The limited data from India present a distinct spectrum of infection in transplant recipients with high incidence of mucormycosis. During COVID-19 outbreak, IFI rate increased and renal transplant recipients acquired mucormycosis earlier than previous studies.

Summary: Maximum data on IFI was available from renal transplant recipients, wherein mucormycosis was the predominant IFI in Indian patients in contrast to invasive candidiasis in majority countries.

The other IFIs had varied spectrum. With the increasing number of SOTs being performed and the already persisting high burden of IFI in India, there is an urgent need of larger prospective studies on epidemiology of IFI in transplant recipients.

2. **Evaluation of antifungal susceptibility and clinical characteristics in fungal keratitis in a tertiary care center in North India**

Murugesan Vanathi[1], Ravinder Naik[1], Navneet Sidhu[1], Nishat Hussain Ahmed[2], Noopur Gupta[1], Radhika Tandon[1]

[1]Cornea, Lens and Refractive Surgery Services, Dr. R P Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, India, [2]Ocular Microbiology Services, Dr. R P Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, India

Abstract

Purpose: To study the antifungal susceptibility of common corneal pathogenic fungi to antifungal agents in the North Indian population.

Methods: Prospective study of the antifungal sensitivity testing (natamycin, amphotericin B, voriconazole, itraconazole, fluconazole, posaconazole, caspofungin, micafungin) of fungal isolates from 50 cases of culture positive fungal keratitis by using E test method. Details noted included demographic data, visual acuity, clinical details, grade of keratitis, healing time, and success in medical management.

Results: Of 50 patients with fungal keratitis (mean age: 40.28 ± 16.77 years), 12 eyes healed within 3 weeks, 14 had a delayed

healing response, and 24 had chronic keratitis. Among the 15 cases of *Fusarium* isolates, 93.3% were sensitive to natamycin, while 40% to amphotericin B; 66.6% to voriconazole, 13.4% to itraconazole and fluconazole each. 80% of *Fusarium* cases (n = 12) showed susceptibility to posaconazole. Among *Aspergillus flavus* isolates, 53.4% (n = 8) were sensitive to natamycin, with only 40% (n = 7) showing sensitivity to amphotericin B and good susceptibility to azoles. MIC against susceptible *Fusarium* spp. for natamycin was 3-16 µg/mL, amphotericin B: 1-8 µg/mL, voriconazole: 0.5-1.5 µg/mL, itraconazole: 0.5-12 µg/mL, posaconazole: 0.094-1.5 µg/mL. MIC against *Aspergillus flavus* was natamycin: 8-32 µg/mL, amphotericin B: 0.5-16 µg/mL, voriconazole: 0.025-4 µg/mL, itraconazole: 0.125-8 µg/mL, posaconazole: 0.047-0.25 µg/mL; against *Aspergillus niger* isolates, to natamycin was 6 µg/mL (n=1), amphotericin B 8-12 µg/mL (n = 3), voriconazole: 0.125-0.19 µg/mL (n = 3), itraconazole: 0.38-0.75 µg/mL, posaconazole: 0.064-0.19 µg/mL and against *Aspergillus fumigatus* (n = 1), was natamycin4 µg/mL, amphotericin B - 8 µg/mL, voriconazole 0.25 µg/mL, itraconazole 1 µg/mL, and posaconazole 0.19 µg/mL. MIC against susceptible *Acremonium* spp. for natamycin was 1.5-16 µg/mL, amphotericin B: 0.5-8 µg/mL, voriconazole: 0.19-3 µg/mL, itraconazole: 0.125 µg/mL, posaconazole: 0.125-0.5 µg/mL and against susceptible *Curvularia* was natamycin 0.75-4 µg/mL, amphotericin B 0.5-1 µg/mL, voriconazole 0.125-0.19 µg/mL, itraconazole 0.047-0.094 µg/mL, posaconazole 0.047-0.094 µg/mL. MIC against *Mucor* spp.+ *Rhizopus* spp. (n = 1) was natamycin: 8 µg/mL, amphotericin B: 0.75 µg/mL, posaconazole: 1.5 µg/mL. MIC against of Alternaria (n = 1) was voriconazole: 0.19 µg/mL, posaconazole: 0.094 µg/mL. MIC against *Penicillium* (n=1) was natamycin: 8 µg/mL, voriconazole: 0.25 µg/mL, itraconazole: 0.5 µg/mL, and Posaconazole: 0.125 µg/mL.

Conclusion: Our observations highlight the variations in susceptibility to antifungal agents. Posaconazole seems to be effective with low MIC against common corneal pathogenic fungal isolates.

3. **Post Covid-19 Acute Invasive Fungal Rhinosinusitis (AIFR): A Study of Histopathological Findings After FESS in Radiologically Diagnosed AIFR**

Payal R Vadher[1,2], Sejal N Mistry[1], Ankita Vasani[1]

[1]ENT Department, Civil Hospital, PDU Medical College, Rajkot, Gujarat India, [2]ENT Department, All India Institute of Medical Sciences (AIIMS), Rajkot, Gujarat India

Abstract

COVID-19 pandemic has led to a concerning surge of post-COVID-19 AIFR. Mucormycosis (BLACK fungus) is a rare but severe and life-threatening fungal infection caused by mucormycetes, a family of moulds. More than 49,000 cases of AIFR were reported in three months in India. It primarily affects diabetics and spreads from the nasal cavity and paranasal sinuses (PNS). It also involves eye, palate, or brain. It is diagnosed clinically followed by radiological and pathological findings. We aimed to compare and analyse the pre-operative imaging with postoperative histopathological findings. The study was conducted in ENT department of tertiary care hospital, Rajkot. 200 patients were randomly selected who were presented to ENT OPD with clinically suspected Post COVID-19 AIFR. All patients underwent detailed ENT examination and radiological modality like MRI PNS, Brain, and Orbit. After proper pre-op evaluation, all patients underwent Functional Endoscopic Sinus Surgery (FESS). MRI findings were confirmed with that of histopathological findings done on KOH mount. All the patients were showing AIFR on MRI findings whereas 49% of patients had mucormycosis on Histopathology. Various other fungal infections like aspergillosis (7%), candidiasis (1.5%) were also found on HPE. 9% of patients showed combined infection with mucor and aspergillus species. Rest of the patients showed non-fungal rhinosinusitis. Inflow

of the epidemic, plenty of patients were shown invasive fungal sinusitis in MRI patterns whereas many of them were HPE negative. Thus this study was done to know the efficacy of radiological features with pathological diagnosis. We have considered both procedures standard in our study.

4. **Inferring Therapeutic Targets in *Candida albicans* and Possible Inhibition through Natural Products: A Binding and Physiological Based Pharmacokinetics Snapshot**

Zarrin Basharat[1], Kanwal Khan[2], Khurshid Jalal[3], Sulaiman Mohammed Alnasser[4], Sania Majeed[1], Marium Zehra[1]

[1]Jamil-ur-Rahman Center for Genome Research, Dr. Panjwani Center for Molecular Medicine and Drug Research, International Center for Chemical and Biological Sciences, University of Karachi, Karachi 75270, Pakistan, [2]Dr. Panjwani Center for Molecular Medicine and Drug Research, International Center for Chemical and Biological Sciences, University of Karachi, Karachi 75270, Pakistan, [3]HEJ Research Institute of Chemistry, International Center for Chemical and Biological Sciences, University of Karachi, Karachi 75270, Pakistan, [4]Department of Pharmacology and Toxicology, Unaizah College of Pharmacy, Qassim University, Buraydah 52571, Saudi Arabia

Abstract

Despite being responsible for invasive infections, fungal pathogens have been underrepresented in computer aided therapeutic target mining and drug design. Excess of *Candida albicans* causes candidiasis, causative of thrush and vaginal infection due to off-balance. In this study, we attempted to mine drug targets (n = 46) using a subtractive proteomic approach in this pathogenic yeast and screen natural products with inhibition potential against fructose-bisphosphate aldolase (FBA) of the C. albicans. The top compound selected on the basis of best docking score from traditional Indian medicine/Ayurvedic library was (4-Hydroxybenzyl) thiocarbamic acid, from the ZINC FBA inhibitor library was ZINC13507461 (IUPAC name: [(2R)-2-hydroxy-3-phosphonooxypropyl] (9E,12E)-octadeca-9,12-dienoate), and from traditional Tibetan medicine/Sowa rigpa was Chelerythrine (IUPAC name: 1,2-Dimethoxy-12-methyl-9H-[1,3]benzodioxolo[5,6-c]phenanthridin-12-ium), compared to the control (2E)-1-(4-nitrophenyl)-2-[(4-nitrophenyl)methylidene] hydrazine. No Ames toxicity was predicted for prioritized compounds while control depicted this toxicity. (4-Hydroxybenzyl) thiocarbamic acid showed hepatotoxicity, while Chelerythrine depicted hERG inhibition, which can lead to QT syndrome, so we recommend ZINC13507461 for further testing in lab. Pharmacological based pharmacokinetic modeling revealed that it has low bioavailability and hence, absorption in healthy state. In cirrhosis and renal impairment, absorption and plasma accumulation increased so we recommend further investigation into this occurrence and recommend high dosage in further tests to increase bioavailability.

5. **Coumarin-based combined computational study to design novel drugs against *Candida albicans***

Akhilesh Kumar Maurya, Nidhi Mishra

Chemistry Laboratory, Department of Applied Sciences, Indian Institute of Information Technology, Allahabad, Prayagraj, 211015, India

Abstract

Candida species cause the most prevalent fungal illness, candidiasis. *Candida albicans* is known to cause bloodstream infections. This species is a commensal bacterium, but it can cause hospital-acquired diseases, particularly in COVID-19 patients with impaired immune

systems. *Candida* infections have increased in patients with acute respiratory distress syndrome. Coumarins are both naturally occurring and synthetically produced. In this study, the biological activity of 40 coumarin derivatives was used to create a three-dimensional quantitative structure activity relationship (3D-QSAR) model. The training and test minimum inhibitory concentration values of *C. albicans* active compounds were split, and a regression model based on statistical data was established. This model served as a foundation for the creation of coumarin derivative QSARs. This is a unique way to create new therapeutic compounds for various ailments. We constructed novel structural coumarin derivatives using the derived QSAR model, and the models were confirmed using molecular docking and molecular dynamics simulation.

6. **A Soluble Tetrazolium-Based Reduction Assay to Evaluate the Effect of Antibodies on *Candida tropicalis* Biofilms**

Pankaj Chandley[#], Priyanka Subba[#], Soma Rohatgi

Department of Biosciences and Bioengineering, Indian Institute of Technology Roorkee.

#Contributed equally.

Abstract

Candida species are the fourth-most common cause of systemic nosocomial infections. Systemic or invasive candidiasis frequently involves biofilm formation on implanted devices or catheters, which is associated with increased virulence and mortality. Biofilms produced by different *Candida* species exhibit enhanced resistance against various antifungal drugs. Therefore, there is a need to develop effective immunotherapies or adjunctive treatments against *Candida* biofilms. While the role of cellular immunity is well established in anti-*Candida* protection, the role of humoral immunity has been studied less. It has been hypothesized that inhibition of biofilm formation and maturation is one of the major functions of protective antibodies, and *Candida* albicans germ tube antibodies (CAGTA) have been shown to suppress in vitro growth and biofilm formation of C. albicans earlier. This paper outlines a detailed protocol for evaluating the role of antibodies on biofilms formed by *C. tropicalis*. The methodology for this protocol involves *C. tropicalis* biofilm formation in 96-well microtiter plates, which were then incubated in the presence or absence of antigen-specific antibodies, followed by a 2,3-bis(2-methoxy-4-nitro-5-sulfophenyl)-5-carboxanilide-2H-tetrazolium (XTT) assay for measuring the metabolic activity of fungal cells in the biofilm. The specificity was confirmed by using appropriate serum controls, including Sap2-specific antibody-depleted serum. The results demonstrate that antibodies present in the serum of immunized animals can inhibit *Candida* biofilm maturation in vitro. In summary, this paper provides important insights regarding the potential of antibodies in developing novel immunotherapies and synergistic or adjunctive treatments against biofilms during invasive candidiasis. This in vitro protocol can be used to check the effect of potential new antifungal compounds on the metabolic activity of *Candida* species cells in biofilms.

7. **Quantitative B and T cell abnormalities in four patients presenting with mucormycosis and prior asymptomatic COVID-19 infection**

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Abstract

India saw an unprecedented and rapid rise of invasive coronavirus-associated mucormycosis (CAM) during the delta COVID-19 surge. There is little known about the pathophysiology and if there is a direct causation between the COVID-19 infection and invasive CAM. While the traditional risk factors such as uncontrolled diabetes and other immunocompromising conditions are recognised, there could be several COVID-19-induced phenomena that may predispose the patients to develop CAM and are yet unrecognised. It has been proposed that prior severe COVID-19 is associated with invasive CAM. This could be due to the increased use of immunomodulators or the direct effects of the COVID-19 infection. We report four patients with CAM during the delta surge who did not have prior known COVID-19 infection but on subsequent testing had positive antibodies suggesting past asymptomatic infection. We report the quantitative abnormalities in lymphocyte subsets in all four patients and report CD19+ B cell lymphopenia and reduced percentage of CD27+ CD45RA+ naïve helper T cells. CAM may occur in patients after asymptomatic COVID-19 infection, in the absence of systemic corticosteroid and immunomodulator use, and may reflect underlying immune abnormalities possibly attributable to or unmasked by prior COVID-19 infection.

8. **Size and Zeta Potential Clicked Germination Attenuation and Anti-Sporangiospores Activity of PEI-Functionalized Silver Nanoparticles against COVID-19 Associated Mucorales (Rhizopus arrhizus)**

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Abstract

The SARS-CoV-2 infections in Indian people have been associated with a mucormycotic fungal infection caused by the filamentous fungi *Rhizopus arrhizus*. The sporangiospores of *R. arrhizus* are omnipresent in the environment and cause infection through inhalation or ingestion of contaminated air and foods. Therefore, the anti-sporangiospore activity of polyethyleneimine functionalized silver nanoparticles (PEI-f-Ag-NPs) with variable size and surface charge as a function of the molecular weight of PEI was explored. The results showed that both PEI-f-AgNP-1 and PEI-f-AgNP-2, potentially, attenuated the germination and reduced the viability of sporangiospores. Furthermore, the results showed that the minimum inhibitory concentration (MIC) values of both PEI-f-AgNP-1 and PEI-f-AgNP-2 (1.65 and 6.50 μg/mL, respectively) were dependent on the nanoparticle size and surface ζ potentials. Similarly, the sporangiospore germination inhibition at MIC values was recorded, showing 97.33% and 94% germination inhibition, respectively, by PEI-f-AgNP-1 and 2 within 24 h, respectively. The confocal laser scanning microscopy, SEM-EDS, and confocal Raman spectroscopy investigation of PEI-f-Ag-NPs treated sporangiospores confirmed size and surface charge-dependent killing dynamics in sporangiospores. To the best of our knowledge, this is the first investigation of the

polyethyleneimine functionalized silver nanoparticle-mediated size and surface charge-dependent anti-sporangiospore activity against *R. arrhizus*, along with a possible antifungal mechanism.

9. Molecular investigations on *Candida glabrata* clinical isolates for pharmacological targeting

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Abstract

Prevalence of drug resistant *C. glabrata* strains in hospitalized immune-compromised patients with invasive fungal infections has increased at an unexpected pace. This has greatly pushed researchers in identification of mutations/variations in clinical isolates for better assessment of the prevailing drug resistance trends and also for updating of antifungal therapy regime. In the present investigation, the clinical isolates of *C. glabrata* were comprehensively characterized at a molecular level using metabolic profiling and transcriptional expression analysis approaches in combination with biochemical, morphological and chemical profiling methods. Biochemically, significant variations in azole susceptibility, surface hydrophobicity, and oxidative stress generation were observed among the isolates as compared to wild-type. The 1H NMR profiling identified 18 differential metabolites in clinical strains compared to wild-type and were classified into five categories, that include: sugars (7), amino acids and their derivatives (7), nitrogen bases (3) and coenzymes (1). Transcriptional analysis of selective metabolic and regulatory enzymes established that the major differences were found in cell membrane stress, carbohydrate metabolism, amino acid biosynthesis, ergosterol pathway and turnover of nitrogen bases. This detailed molecular level/metabolic fingerprint study is a useful approach for differentiating pathogenic/clinical isolates to that of wild-type. This study comprehensively delineated the differential cellular pathways at a molecular level that have been re-wired by the pathogenic clinical isolates for enhanced pathogenicity and virulence traits.

10. Luliconazole Nail Lacquer for the Treatment of Onychomycosis: Formulation, Characterization and In Vitro and Ex Vivo Evaluation

Deepa Dehari[1], Abhishesh Kumar Mehata[1], Vishnu Priya[1], Dharmnath Parbat[1], Deepak Kumar[2], Anand Kumar Srivastava[3], Sanjay Singh[1,4], Ashish Kumar Agrawal[5]

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Abstract

Onychomycosis is the most common fungal infection of the nail affecting the skin under the fingertips and the toes. Currently, available therapy for onychomycosis includes oral and topical therapies, either alone or in combination. Oral antifungal medication has been associated with poor drug bioavailability and potential gastrointestinal and systemic side effects. The objective of this study was to prepare and evaluate the luliconazole nail lacquer (LCZ-NL) for the effective treatment of onychomycosis. In the current work, LCZ-NL was formulated in combination with penetration enhancers to overcome poor penetration. A 32 full factorial formulation design of experiment (DOE) was applied for optimization of batches with consideration of dependent (drying time, viscosity, and rate of drug diffusion) and independent (solvent ratio and film former ratio) variables. The optimized formulation was selected based on drying time, viscosity, and rate of drug diffusion. The optimized formulation was further evaluated for % non-volatile content assay, smoothness of flow, water resistance, drug content, scanning electron microscope (SEM), atomic force microscope (AFM), X-ray diffraction (XRD), differential scanning calorimetry (DSC), in vitro drug release, ex vivo transungual permeation, antifungal efficacy, and stability study. The optimized LCZ-NL contained 70:30 solvent ratio and 1:1 film former ratio and was found to have ~ 1.79-fold higher rate of drug diffusion in comparison with LULY™. DSC and XRD studies confirmed that luliconazole retains its crystalline property in the prepared formulation. Antifungal study against *Trichophyton* spp. showed that LCZ-NL has comparatively higher growth inhibition than LULY™. Hence, developed LCZ-NL can be a promising topical drug delivery system for treating onychomycosis.

11. Faster and accurate identification of clinically important *Trichosporon* using MALDI TOF MS

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Abstract

Purpose: *Trichosporon* species are emerging human pathogens, accounting for the second most common cause of non-candidal mycosis. Rapid and reliable identification of these agents allows a better understanding of their epidemiology and therapeutic management. The Matrix-Assisted Laser Desorption Ionization-Time-of-Flight Mass Spectrometry (MALDI-TOF MS) technique has the potential to be precise, fast and cost-effective. However, the precision of identification totally depends upon the type of protein extraction method used and embedded database in the system. Our objectives were to standardize the protein extraction technique and expand the present Bruker database by creating an in-house database and validating it with diverse clinical *Trichosporon* species of Indian origin.

Methods: Two different protein extraction protocols (on-plate and off-plate) were evaluated. The off-plate protocol was finalized for the identification. MALDI TOF MS with the existing Bruker database was evaluated for its ability to identify a total of 79 intergenic spacer 1 (IGS1) gene sequence confirmed clinical isolates of 5 different *Trichosporon* species.

Results: As outcome, off plate protocol yielded higher accuracy (73% on the species level and 95% on the genus level) than on-plate (25% on the genus level) in terms of log scores. The existing database for *Trichosporon* species was enriched with 28 sequence confirmed isolates, which improved accuracy from 73% to 100% and were identified up to species level with a log score >2.3.

Conclusions: Used with standardized protein-extraction protocol along with an expanded database, MALDI-TOF MS could be a rapid and reliable approach to identify clinical *Trichosporon* species routinely in the laboratory.

12. **Comparative evaluation of host immune response and cytokine signature pertaining to Th1 and Th2 immune arms in serum and tissue among patients of acute localised vs. chronic disseminated dermatophytosis**

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Abstract

Background: India is witnessing an epidemic of dermatophytosis. The role of host immune response against fungi in chronicity and dissemination is topic of ongoing research. We conducted cross-sectional comparative study to determine the difference in Th1 (IFN-γ) and Th2 (IL4) response in serum and tissue between acute and localised vs. chronic and disseminated cases.

Methods: Patients (18-60 years) were divided in two groups-group A (n = 114, BSA <5%, single anatomic site, duration <6 months, n = 118) and group B (n = 107 BSA >10%, > one anatomic site, duration >12 months, n = 118). Clinical parameters along with serum levels of IgE, IL-4 and IFN-γ and expression of IL4 and IFN-γ in dermal infiltrate were compared between group.

Results: Trichophyton mentagrophytes complex was commonest causative fungi. Serum levels of IgE were significantly higher (median A-539.2, B-2901.0, p < .001) whereas levels IL-4(median A-21.3, B-20.4, p < .001) and IFN-γ(median A-9.6, B-5.1, p < .001) were significantly lower in chronic cases. Expression of IL-4 was observed in most biopsy specimens in both groups without any difference in intensity of staining. Expression of IFN-γ was not detected in all but one specimen across both the groups. Severe itching (OR:0.050, CI:0.018, 0.139, p < .001), sign of topical steroid abuse (OR:0.203,CI:0.077, 0.537; p = .001), ↓IFN-γ (OR:4.683, CI:1.634, 13.418; p = .004) correlated significantly and independently with chronic dermatophytosis.

Conclusion: Our study shows chronic and disseminated cases of dermatophytosis differ immunologically in terms of higher IgE, and lower IL4 and IFN-γ. Expression of IL4 is present in tissue of both acute, localised and chronic disseminated cases. Expression of IFN-γ cannot be established in our study.

13. **Targeted specific inhibition of bacterial and *Candida* species by mesoporous Ag/Sn-SnO2 composite nanoparticles: *in silico* and *in vitro* investigation**

Monica Pandey[1], Kirti Wasnik[2], Shubhra Gupta[2], Monika Singh[2], Sukanya Patra[2], Premshankar Gupta[2], Divya Pareek[2], Somedutta Maity[1], Ragini Tilak[3], Pradip Paik[2]

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Abstract

Invasive bacterial and fungal infections have notably increased the burden on the health care system and especially in immune compromised patients. These invasive bacterial and fungal species mimic and interact with the host extracellular matrix and increase the adhesion and internalization into the host system. Further, increased resistance of traditional antibiotics/antifungal drugs led to the demand for other therapeutics and preventive measures. Presently, metallic nanoparticles have wide applications in health care sectors. The present study has been designed to evaluate the advantage of Ag/Sn-SnO2 composite nanoparticles over the single oxide/metallic nanoparticles. By using in silico molecular docking approaches, herein we have evaluated the effects of Ag/Sn-SnO2 nanoparticles on adhesion and invasion responsible molecular targets such as LpfD (*E. coli*), Als3 (*C. albicans*) and on virulence/resistance causing PqsR (*P. aeruginosa*), RstA (Bmfr) (*A. baumannii*), FoxA (*K. pneumonia*), Hsp90 and Cyp51 (*C. albicans*). These Ag/Sn-SnO2 nanoparticles exhibited higher antimicrobial activities, especially against the *C. albicans*, which are the highest ever reported results. Further, Ag/Sn-SnO2 NPs exhibited interaction with the heme proionate residues such as Lys143, His468, Tyr132, Arg381, Phe105, Gly465, Gly464, Ile471 and Ile304 by forming hydrogen bonds with the Arg 381 residue of lanosterol 1 4α-demethylase and increased the inhibition of the *Candida* strains. Additionally, the Ag/Sn-SnO2 nanoparticles exhibited extraordinary inhibitory properties by targeting different proteins of bacteria and *Candida* species followed by several molecular pathways which indicated that it can be used to eliminate the resistance to traditional antibiotics.

14. **A quality improvement initiative to improve the appropriateness of candidemia management by the implementation of a comprehensive candidemia care bundle at a tertiary care hospital in South India: Results of a quasi-experimental study**

Merlin Moni[1], Neeraj Sidharthan[2], Sangita Sudhir[3], Binny Prabhu[4], Vrinda Nampoothiri[3], Jini James[3], Jeslyn Mary Philip[3], Jisha Thomas[3], Remya Antony[3], Zubair Umer Mohamed[5], Anil Kumar[6], Preetha Prasanna[1], Fabia Edathadathil[3], Sanjeev Singh[3], Dipu Sathyapalan[1]

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Abstract

Management of candidemia in developing countries like India encounters laxity in appropriate clinical management and challenges in terms of healthcare capacity, despite its association with high morbidity and mortality. Our study aims to evaluate the impact of a comprehensive candidemia care bundle implementation on appropriateness of therapy and major clinical outcomes. The single-center, quasi-experimental study conducted at a south Indian tertiary care center included adult patients diagnosed with candidemia. Following a retrospective review of candidemia patients of the pre-implementation period (January 2013-December 2015), the hospital

antifungal stewardship team instituted a clinical pharmacist driven comprehensive candidemia care bundle for candidemia patients during the post-implementation period (October 2017-2019) and its impact on appropriateness of antifungal prescriptions and inpatient mortality was evaluated. The study included 175 patients with candidemia, comprising of 103 patients in the pre-implementation period and 72 patients in the post-implementation period. Appropriateness of antifungal prescriptions rose to 65% during post-implementation period from 30% observed in pre-implementation phase (P = .0005). The inhospital mortality rate reduced from 40% in the pre-implementation phase to 36% in the post-implementation phase, recording a 10% reduction over 2 years post-implementation (P = .26). No significant difference was observed in terms length of stay (P = .17). Our study demonstrates the successful implementation of an antifungal stewardship led comprehensive care bundle in a low middle income countries setting. The results of our study will have profound implications in improving the appropriateness of management of candidemia and feasibility of scaling up to wider settings could be explored.

15. Antibacterial metabolites from an unexplored strain of marine fungi *Emericellopsis minima* and determination of the probable mode of action against *Staphylococcus aureus* and methicillin-resistant *S. aureus*

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Abstract

Increasing prevalence of drug resistance has led researchers to focus on discovering new antibacterial agents derived from the marine biome. Although ample studies have investigated marine fungi for their bioactive metabolites with hopeful prospects in drug discovery. The present study was aimed to isolate/ identify potential antimethicillin-resistant *Staphylococcus aureus* compounds producing marine fungal strain from the Indian marine environment. The effective anti-MRSA compound was produced by a marine fungal strain designated as D6. The D6 strain exhibited 99% similarity to *Emericellopsis minima* based on 18S rRNA gene analysis. The culture conditions of *E. minima* D6 were optimized using nutritional and environmental parameters for enhanced anti-MRSA compound production. The agar well diffusion assay was used to determine the inhibition zone diameter of the crude extract against S. aureus and methicillin-resistant S. aureus, whereas the broth microdilution method was used to determine their minimum inhibitory concentration (MIC) active fraction. MIC values of the ethyl acetate fraction ranged from 0.8 to 1 mg/mL. SEM analysis revealed that the ethyl acetate fraction induces deep craters in methicillin-resistant *S. aureus*. Further, GC-MS analysis confirmed the occurrence of a total of 15 major compounds in active ethyl acetate fraction. Some of the major antibacterial compounds included cyclopentanol, isothiazole, benzoic acid, pyrrolo[1,2-a] pyrazine-1,4-dione, and hexahydro. These findings suggest that the marine fungi of *E. minima* can be a valuable candidate for prospecting antibiotics and an alternative complementary strategy for drug-resistant bacterial infections.

16. Understanding the science of fungal endophthalmitis - AIOS 2021 Sengamedu Srinivas Badrinath Endowment Lecture

Taraprasad Das[1], Joveeta Joseph[2], Saumya Jakati[3], Savitri Sharma[2], Thirumurthy Velpandian[4], Srikant K Padhy[5], Vipin A Das[6], Sisinthy Shivaji[2], Sameera Nayak[7], Umesh C Behera[5], Dilip K Mishra[3], Jaishree Gandhi[2], Vivek P Dave[1], Avinash Pathengay[8]

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Abstract

Fungal endophthalmitis is a potentially blinding condition. It is more often reported from Asia, including India. The incidence is lower than bacterial endophthalmitis. But it is relatively more challenging to treat than bacterial endophthalmitis. Many eyes may need therapeutic keratoplasty and/or evisceration. The current mainstays of treatment are vitrectomy irrespective of the presenting vision, intravitreal antifungal agents, and systemic therapy; additionally, the patients could require prolonged treatment with repeat vitreous surgeries and intravitreal injections. Difficulty in clinical diagnosis, delay in microbiological culture, and limited options of antifungal drugs make the treatment more difficult and less rewarding. Three common fungi causing endophthalmitis are *Aspergillus, Fusarium*, and *Candida*. The former two are molds, often identified in exogenous endophthalmitis, postoperative and traumatic; the latter is yeast and is more often identified in endogenous endophthalmitis. A faster diagnosis with newer molecular microbiological technologies might help institute treatment earlier than it is currently possible. A target trial using big data from different regions of the world might emulate a randomized clinical trial to design a definite treatment strategy. Given fewer antifungal drugs, one must be mindful of antifungal stewardship to prevent resistance to the existing drugs.

17. Sensitivity and specificity of potassium hydroxide and calcofluor white stain to differentiate between fungal and *Pythium* filaments in corneal scrapings from patients of Pythium keratitis

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Abstract

Purpose: To assess the sensitivity of potassium hydroxide and calcofluor white (KOH+CFW) mount in the diagnosis of *Pythium* keratitis and concordance among microbiologists.

Methods: Three microbiologists evaluated the microscopic images of KOH + CFW mounts of confirmed cases of Pythium and fungal keratitis seen between January 2019 and February 2021. The filaments were compared using specific differentiating features. The sensitivity and specificity of KOH + CFW in diagnosing Pythium infection were evaluated along with concordance among the microbiologists.

Results: Sixty consecutive cases with confirmed growth of fungus or *Pythium insidiosum* (n = 29) were evaluated. The sensitivity of KOH + CFW in the correct identification of Pythium filaments ranged from 79.3% to 96.5% among three microbiologists. There was good interobserver (k = 0.76-0.90) and intraobserver (k = 0.70-0.97)

agreements among three microbiologists. The differentiating findings (P < 0.0001) suggestive of *Pythium* filaments were the absence of septae in 23 (79.3%) and collapsed walls in 22 (75.9%) cases.

Conclusion: KOH + CFW has good sensitivity and specificity in the diagnosis of Pythium keratitis with good interobserver and intraobserver concordance.

18. **Phytolectin nanoconjugates in combination with standard antifungals curb multi-species biofilms and virulence of vulvovaginal candidiasis (VVC) causing Candida albicans and non-albicans Candida**

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Abstract

Vulvovaginal candidiasis (VVC) is a commonly occurring yeast infection caused by *Candida* species in women. Among *Candida* species, *C. albicans* is the predominant member that causes vaginal candidiasis followed by *Candida glabrata*. Biofilm formation by *Candida albicans* on the vaginal mucosal tissue leads to VVC infection and is one of the factors for a commensal organism to get into virulent form leading to disease. In addition to that, morphological switching from yeast to hyphal form increases the risk of pathogenesis as it aids in tissue invasion. In this study, jacalin, a phytolectin complexed copper sulfide nanoparticles (NPs) have been explored to eradicate the mono and mixed species biofilms formed by fluconazole-resistant *C. albicans* and *C. glabrata* isolated from VVC patients. NPs along with standard antifungals like micafungin and amphotericin B have been evaluated to explore interaction behavior and we observed synergistic interactions between them. Microscopic techniques like light microscopy, phase contrast microscopy, scanning electron microscopy, confocal laser scanning microscopy were used to visualize the inhibition of biofilm by NPs and in synergistic combinations with standard antifungals. Real-time PCR analysis was carried out to study the expression pattern of the highly virulent genes which are responsible for yeast to hyphal switch, drug resistance and biofilm formation upon treatment with NPs in combination with standard antifungals. The current study shows that lectin-conjugated NPs with standard antifungals might be a different means to disrupt the mixed species population of *Candida* spp. that causes VVC.

19. **Comparative Host-Pathogen Interaction Analyses of SARS-CoV2 and *Aspergillus fumigatus*, and Pathogenesis of COVID-19-Associated Aspergillosis**

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Abstract

COVID-19 caused a global catastrophe with a large number of cases making it one of the major pandemics of the human history. The clinical presentations of the disease are continuously challenging healthcare workers with the variation of pandemic waves and viral variants. Recently, SARS-CoV2 patients have shown increased occurrence of invasive pulmonary aspergillosis infection even in the absence of traditional risk factors. The mechanism of COVID-19-associated aspergillosis is not completely understood and therefore, we performed this system biological study in order to identify mechanistic implications of aspergillosis susceptibility in COVID-19 patients and the important targets associated with this disease. We performed host-pathogen interaction (HPI) analysis of SARS-CoV2, and most common COVID-19-associated aspergillosis pathogen, *Aspergillus fumigatus*, using in silico approaches. The known host-pathogen interactions data of SARS-CoV2 was obtained from BIOGRID database. In addition, *A. fumigatus* host-pathogen interactions were predicted through homology modeling. The human targets interacting with both pathogens were separately analyzed for their involvement in aspergillosis. The aspergillosis human targets were screened from DisGeNet and GeneCards. The aspergillosis targets involved in both HPI were further analyzed for functional overrepresentation analysis using PANTHER. The results indicate that both pathogens interact with a number of aspergillosis targets and altogether they recruit more aspergillosis targets in host-pathogen interaction than alone. Common aspergillosis targets involved in HPI with both SARS-CoV2 and *A. fumigatus* can indicate strategies for the management of both conditions by modulating these common disease targets.

20. **Predictive Factors for Resolution of Dematiaceous Fungal Keratitis**

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Abstract

Purpose: To ascertain the clinicomicrobiological correlation and evaluate the prognostic factors associated with medical resolution in cases of Curvularia, Alternaria, and Scedosporium keratitis.

Methods: A retrospective review of clinical and microbiological records of culture-proven cases of *Curvularia, Alternaria*, and *Scedosporium* keratitis from 2017 to 2019 was performed. Multivariate logistic regression analyses were performed to assess the predictive factors for medical resolution.

Results: There were a total of 79 eyes of 79 patients. Among these, there were 56 (70.8%), 15 (18.9%), and 8 (10.1%) patients with *Curvularia, Scedosporium*, and *Alternaria* keratitis, respectively. Clinical resolution with medical treatment was achieved in 46 of 56 (82.1%) patients with *Curvularia* keratitis, 8 of 15 (53.3%) patients with *Scedosporium*, and 7 of 8 (87.5%) patients with *Alternaria* keratitis. In comparison between *Curvularia* and *Scedosporium*, macroscopic pigmentation [18/56 (32.1%)] of anterior stromal plaque-like infiltrate [20/56 (35.7%)] was clinically more in cases with *Curvularia*, whereas larger diameter of the infiltrate, P = 0.002, posterior stromal infiltrate (40%), P = 0.03, and hypopyon, P = 0.009, were more common with *Scedosporium*. Multivariate logistic regression analysis, by backward elimination, showed that maximum dimension of the infiltrate (P = 0.01; odds ratio = 0.52, 95% confidence

interval, 0.31-0.86) and presence of a hypopyon (P = 0.02; odds ratio = 0.12, 95% confidence interval, 0.02-0.71) were significant factors that were not favoring medical resolution.

Conclusions: Larger size of the infiltrate, posterior stromal involvement, and presence of a hypopyon are poor prognostic indicators among all 3 species. Variation in species is not a predictor of clinical resolution.

21. **Molecular diagnosis of rhino-orbital mucormycosis in a COVID-19 setting**

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Abstract

Purpose: Mucormycosis is a severe fungal infection caused by species of the order Mucorales. Early and accurate diagnosis is a prerequisite in the management of the disease. In the present study, we evaluated and compared two PCR-based techniques for the diagnosis and identification of mucormycosis in patients with rhino-orbital mucormycosis (ROM) post-COVID-19.

Methods: Diagnosed clinically and radiologically, 25 patients of ROM were included in the study and endoscopically or blind collected nasal swabs or orbital tissues were submitted for microbiological evaluation (direct microscopy + culture) and PCR using primers targeting two different loci (ITS and 28S rDNA region) for diagnosis. All PCR products were further processed for species identification using Sanger sequencing whenever possible.

Result: Of the 25 samples included in the study, 16 samples were positive for presence of fungal filaments by Smear suggestive of Mucorales sp., but only 7/25 grew in culture. ITS-based PCR was able to identify mucormycosis in 7/25 (28%) samples and 28S rDNA PCR showed positivity for 19/25 (76%) samples. *Rhizopus oryzae* was found to be the predominant species in our study. The sensitivity and specificity of 28S rDNA PCR compared to culture were found to be 85.71% and 27.78%, respectively, while for ITS-based PCR, they were 42.86% and 77.78%, respectively.

Conclusions: 28S rDNA-based PCR is a reliable and sensitive method for early diagnosis of mucormycosis. Molecular techniques have shown a promising future to provide quick and effective treatment by accurately identifying the aetiologic agent.

22. **Proteomic profiling of extracellular vesicles derived from ARPE-19 cells challenged with *Aspergillus flavus* and *Candida albicans*: application in fungal endophthalmitis**

Jaishree Gandhi[1,2], Joveeta Joseph[1]

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Abstract

Extracellular vesicles (EVs) are nano-sized-particles that play an important role in cellular cross-talk. The aim of this study was to understand the proteomic cargo of EVs, released by Retinal Pigment Epithelial (RPE) cells challenged with *Candida albicans* (C-CA) and *Aspergillus flavus* (C-AF). EVs were isolated from culture supernatant of retinal cells infected with fungal pathogens and characterized by dynamic light scattering, SEM, and western blot. EV proteome was then evaluated by mass spectrometry (LC-MS/MS). Isolated EVs were approximately 120-150 nm and higher in number in infected group compared to control. Proteomic profiling of EVs from infected cells, showed a total of 419 and 254 differentially expressed proteins, of which 218 were upregulated in C-CA group and 81 proteins were upregulated in C-AF group. Gene ontology revealed majority of proteins associated with transport, cell migration, and in activation of innate immune response. Proteins identified were annexins, calpain, and Sorcin proteins. Additionally, KEGG analysis unveiled involvement of MAPK, HIF-1, and PI3K-AKT signalling pathways. Proteomic results indicate that EVs cargo derived from fungal-infected retinal cells can activate immune signalling pathways and might contribute to the pathogenesis of endophthalmitis, indicating the potential use of EVs as theranostic marker for management of fungal infections.

23. **A Novel Deep Learning-Based Black Fungus Disease Identification Using Modified Hybrid Learning Methodology**

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Abstract

Currently, countries across the world are suffering from a prominent viral infection called COVID-19. Most countries are still facing several issues due to this disease, which has resulted in several fatalities. The first COVID-19 wave caused devastation across the world owing to its virulence and led to a massive loss in human lives, impacting the country's economy drastically. A dangerous disease called mucormycosis was discovered worldwide during the second COVID-19 wave, in 2021, which lasted from April to July. The mucormycosis disease is commonly known as "black fungus," which belongs to the fungus family Mucorales. It is usually a rare disease, but the level of destruction caused by the disease is vast and unpredictable. This disease mainly targets people already suffering from other diseases and consuming heavy medication to counter the disease they are suffering from. This is because of the reduction in antibodies in the affected people. Therefore, the patient's body does not have the ability to act against fungus-oriented infections. This black fungus is more commonly identified in patients with coronavirus disease in certain country. The condition frequently manifests on skin, but it can also harm organs such as eyes and brain. This study intends to design a modified neural network logic for an artificial intelligence (AI) strategy with learning principles, called a hybrid learning-based neural network classifier (HLNNC). The proposed method is based on well-known techniques such as convolutional neural network (CNN) and support vector machine (SVM). This article discusses a dataset containing several eye photographs of patients with and without

black fungus infection. These images were collected from the real-time records of people afflicted with COVID followed by the black fungus. This proposed HLNNC scheme identifies the black fungus disease based on the following image processing procedures: image acquisition, preprocessing, feature extraction, and classification; these procedures were performed considering the dataset training and testing principles with proper performance analysis. The results of the procedure are provided in a graphical format with the precise specification, and the efficacy of the proposed method is established.

24. Microbiological profile and antibiotic susceptibility trends in orbital cellulitis in India: an analysis over 15 years

Joveeta Joseph[1], Roshni Karolia[1], Savitri Sharma[1], Harithaa Choudhary[2], Milind N Naik[2]

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Abstract

Purpose: To report the microbiologic profile and antibiotic susceptibility trends in orbital cellulitis.

Methods: Retrospective review of microbiology records of orbital cellulitis between 2005 and 2019. Orbital pus or conjunctival swab underwent culture for bacteria and fungi and antibiotic susceptibility testing for bacterial isolates. The microbiological profile and trends in antibiotic susceptibility were analyzed over the three study periods: 2005-2009, 2010-2014, and 2015-2019.

Results: Of the 203 patient samples, 189 (93%) were orbital pus samples, and 146 (72%) were culture positive. Organisms included bacteria (167/203, 82.3%), fungi (13/203, 6.4%), and mixed infection (25/203, 10.3%). Among bacteria, 79% were gram positive, with *Staphylococcus aureus* and *Streptococcus* species being commonest, and 21% were gram negative, with *Pseudomonas aeruginosa* and Enterobacteriaceae group being the commonest. *Aspergillus flavus* was the most common fungus isolated. Trend analysis revealed no change in the number of sterile cases and fungal cellulitis. Increase in gram positive bacteria was statistically significant (p = 0.0002) between 2005-2009 and 2015-2019. The increase in gram negative bacteria was statistically significant (p = 0.047) between all three time periods. Susceptibility patterns showed increasing trend of resistance to fluoroquinolones, that reached statistical significance for Ciprofloxacin, Moxifloxacin and Gatifloxacin (p < 0.05). Sterile sample was not found in any of the pediatric (0-16 years) cases (n = 55), compared to 28% in adults.

Conclusion: There was a significant rise in gram positive and negative orbital infections over the 15 year period, with increased resistance to fluoroquinolones. Fungal cellulitis and sterile samples showed a steady trend. Orbital aspirate provides accurate detection of the causative organism.

25. Microbiology Profile of COVID-19-Associated Rhino-Orbital Mucormycosis Pathogens in South India

Esther Sheba[1,2], Savitri Sharma[1,2], Dilip Kumar Mishra[2,3], Tarjani Vivek Dave[2,4], Anasua Ganguly Kapoor[5], Joveeta Joseph[1,2]

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Abstract

This study describes the microbiological and histopathological features of patients with COVID-19-associated rhino-orbital mucormycosis (ROM) seen at the L V Prasad Eye Institute between May and August 2021. Diagnosed clinically and radiologically, 24 patients with ROM were included in the study. Deep nasal swabs or endoscopically collected nasal swabs or orbital tissues were submitted for microbiological evaluation and in vitro susceptibility testing by microbroth dilution for natamycin, amphotericin B, caspofungin, posaconazole, ketoconazole, and voriconazole. Cultures were processed by 28S ribosomal DNA polymerase chain reaction and molecular sequencing. A portion of orbital tissues was also sent for histopathological evaluation. The age of the patients ranged from 27 to 75 (mean 48.58 ± 14.09) years and the majority (79%) were male. Nineteen patients were known to be diabetic prior to developing ROM and 18 patients had recovered from active COVID-19 infection. Thirteen patients had a history of hospitalization during COVID-19 infection and eight received steroids. Of the 24 samples, microbiological evaluation identified *Rhizopus arrhizus* in 12, *Rhizopus microsporus* in 9, *Lichtheimia ramosa* in 2, and *Rhizopus delemar* in 1. Twelve isolates were tested for antifungal susceptibility and all were susceptible to natamycin and amphotericin B. The susceptibility to posaconazole was high, with minimum inhibitory concentration (MIC) <2 μg/mL for 10/12 (84%) isolates, whereas the MIC of other drugs varied. Histopathological examination of tissues showed acute fulminant disease, granuloma formation, and vascular invasion by the fungal pathogens in these specimens. *Rhizopus arrhizus* was predominantly associated with ROM and most isolates were susceptible to amphotericin B and posaconazole. Further studies are needed to corroborate the findings and explain possible underlying links.

26. Cirrhosis and fungal infections-a cocktail for catastrophe: A systematic review and meta-analysis with machine learning

Nipun Verma[1], Shreya Singh[2], Akash Roy[1], Arun Valsan[1], Pratibha Garg[1], Pranita Pradhan[3], Arunaloke Chakrabarti[2], Meenu Singh[3]

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Abstract

Objectives: We evaluated the magnitude and factors contributing to poor outcomes among cirrhosis patients with fungal infections (FIs).

Methods: We searched PubMed, Embase, Ovid and WOS and included articles reporting mortality in cirrhosis with FIs. We pooled the point and relative-risk (RR) estimates of mortality on random-effects meta-analysis and explored their heterogeneity (I 2) on subgroups, meta-regression and machine learning (ML). We assessed the study quality through New-Castle-Ottawa Scale and estimate-asymmetry through Eggers regression. (CRD42019142782).

Results: Of 4345, 34 studies (2134 patients) were included (good/fair/poor quality: 12/21/1). Pooled mortality of FIs was 64.1% (95% CI: 55.4-72.0, I 2 : 87%, p < .01), which was 2.1 times higher than controls (95% CI: 1.8-2.5, I 2 :89%, p < .01). Higher CTP (MD: +0.52, 95% CI: 0.27-0.77), MELD (MD: +2.75, 95% CI: 1.21-4.28), organ failures and increased hospital stay (30 vs. 19 days) were reported

among cases with FIs. Patients with ACLF (76.6%, RR: 2.3) and ICU-admission (70.4%, RR: 1.6) had the highest mortality. The risk was maximum for pulmonary FIs (79.4%, RR: 1.8), followed by peritoneal FIs (68.3%, RR: 1.7) and fungemia (55%, RR: 1.7). The mortality was higher in FIs than in bacterial (RR: 1.7) or no infections (RR: 2.9). Estimate asymmetry was evident (p < 0.05). Up to 8 clusters and 5 outlier studies were identified on ML, and the estimate-heterogeneity was eliminated by excluding such studies.

Conclusions: A substantially worse prognosis, poorer than bacterial infections in cirrhosis patients with FIs, indicates an unmet need for improving fungal diagnostics and therapeutics in this population. ACLF and ICU admission should be included in the host criteria for defining IFIs.

27. Proteomic profiling of *Aspergillus flavus* endophthalmitis derived extracellular vesicles in an *in-vivo* murine model

Jaishree Gandhi[1,2], Milind N Naik[3], Dilip K Mishra[4], Joveeta Joseph[1]

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Abstract

Extracellular Vesicles (EVs) play pivotal roles in cell-to-cell communication, and are involved in potential pathological and physiological cellular processes. The aim of this study was to understand the proteomic cargo of these vesicles, in a murine model of Aspergillus flavus (AF) endophthalmitis. EVs were isolated from A. flavus infected C57BL/6 mice eyes by differential ultracentrifugation at 24 h post infection (p.i) and isolated EVs were characterized by Dynamic Light Scattering (DLS), Scanning Electron Microscopy (SEM), Exocet assay, and western blot. Proteomic profiling of EVs was then evaluated by mass spectrometry (LC-MS/MS) and compared it with control uninfected mice. The average size of the EVs were 180-280 nm by DLS and the number of EVs increased to 1.55×10^{10} in infected mice in comparison to EVs from uninfected eye (1.24×10^9). Western blot was positive for CD9, CD63, and CD81 confirming the presence of EVs. LC-MS/MS analysis, identified 81 differentially expressed proteins, of these 22 were up-regulated and 59 were down-regulated. Gene Ontology (GO) analysis revealed enrichment of lipid metabolism, protein complex binding, and transferase activity, and the proteins associated were Aquaporin-5, CD177 antigen, Solute carrier family-25, and Calcium/calmodulin-dependent protein kinase. Additionally, KEGG pathway analysis indicated that glucagon signalling, metabolic, and PPAR signalling pathway were significantly associated with EVs from A. flavus infected mice eyes. The protein cargo in EVs from A. flavus endophthalmitis provides new insights into the pathogenesis of fungal endophthalmitis and validation of these proteins can serve as diagnostic and/or prognostic biomarkers for patients with a clinical suspicion of fungal endophthalmitis.

28. Immunopathology of COVID-19 and its implications in the development of rhino-orbital-cerebral mucormycosis: a major review

Tarjani Vivek Dave[1], Akshay Gopinathan Nair[2,3], Joveeta Joseph[4], Suzanne K Freitag[5]

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Abstract

Purpose: To present a literature review on various immunopathologic dysfunctions following COVID-19 infection and their potential implications in development of rhino-orbital-cerebral mucormycosis (ROCM).

Methods: A literature search was performed via Google Scholar and PubMed with subsequent review of the accompanying references. Analogies were drawn between the immune and physiologic deviations caused by COVID-19 and the tendency of the same to predispose to ROCM.

Results: Sixty-two articles were reviewed. SARS-CoV-2 virus infection leads to disruption of epithelial integrity in the respiratory passages, which may be a potential entry point for the ubiquitous Mucorales to become invasive. COVID-19 related GRP78 protein upregulation may aid in spore germination and hyphal invasion by Mucorales. COVID-19 causes interference in macrophage functioning by direct infection, a tendency for hyperglycemia, and creation of neutrophil extracellular traps. This affects innate immunity against Mucorales. Thrombocytopenia and reduction in the number of natural killer (NK) cells and infected dendritic cells is seen in COVID-19. This reduces the host immune response to pathogenic invasion by Mucorales. Cytokines released in COVID-19 cause mitochondrial dysfunction and accumulation of reactive oxygen species, which cause oxidative damage to the leucocytes. Hyperferritinemia also occurs in COVID-19 resulting in suppression of the hematopoietic proliferation of B- and T-lymphocytes.

Conclusions: COVID-19 has a role in the occurrence of ROCM due to its effects at the entry point of the fungus in the respiratory mucosa, effects of the innate immune system, creation of an environment of iron overload, propagation of hyperglycemia, and effects on the adaptive immune system.

29. Proteomic profiling of exosomes in a mouse model of *Candida albicans* endophthalmitis

Jaishree Gandhi[1*], Mudigunda V Sushma[2], Aravind Kumar Rengan[2], Milind N Naik[3], Dilip K Mishra[4], Sreedhar Rao Boyinpally[4], Joveeta Joseph[1]

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Abstract

Exosomes play pivotal roles in intercellular communication, and pathophysiological functions. In this study, we aimed to understand the role of exosomal proteome derived from *C. albicans* infected mice (C57BL/6) eyeball. Exosomes were characterized by Dynamic Light Scattering and Western blot, quantified and subjected to LC-MS/MS and cytokine quantification by ELISA. The average size of exosomes was 170-200 nm with number of exosomes amounted to 1.42×10^{10} in infected set compared to control (1.24×10^9). Western

blot was positive for CD9, CD63 and CD81 confirming the presence of exosomes. IL-6, IL1β, TNF-α, and IFN-γ levels were significantly elevated in infected eye at 72 h.p.i. Proteomic analysis identified 42 differentially expressed proteins, of these 37 were upregulated and 5 were downregulated. Gene Ontology (GO) revealed enrichment of cell adhesion, cytoskeleton organisation, and cellular response proteins such as aquaporin-5, gasdermin-A, CD5 antigen-like, Catenin, V-ATPase, and vesicle associated protein. Additionally, KEGG pathway analysis indicated the association of metabolic and carbon signalling pathways with exosomes from *C. albicans* infected eye. The protein cargo in exosomes released during endophthalmitis with *C. albicans* seems to play a unique role in the pathogenesis of the disease and further validations with larger cohort of patients is required to confirm them as biomarkers.

30. **Evaluation of Vitreous Galactomannan and (1, 3) β-D-Glucan Levels in the Diagnosis of Fungal Endophthalmitis in Southern India**

Jaishree Gandhi[1,2], Satyashree Gagan[1], Ashik Mohamed[3], Taraprasad Das[4], Vivek Pravin Dave[4], Joveeta Joseph[1]

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Abstract

Purpose: To evaluate vitreous Galactomannan(GM) and 1,3 β-D-Glucan (BDG) levels in the diagnosis of fungal endophthalmitis, with emphasis on culture-negative cases.

Methods: Vitreous from 31 clinically suspected fungal endophthalmitis patients and 11 controls were evaluated for GM and BDG using ELISA Kits. The Receiver Operating Characteristic (ROC) curves and diagnostic significance was calculated.

Results: The median vitreous GM in culture-positive (60.83pg/ml) and culture-negative (59.9pg/ml) samples were higher than the (51.2pg/ml) control group. The median vitreous BDG in culture-positive (1.47pg/ml) and culture-negative (1.52pg/ml) samples were also similar, and higher than the control group (1.18pg/ml). ROC analysis showed that at a cut-off of 51.35pg/ml, the sensitivity and specificity for GM were 0.88 and 0.73.Similarly, for BDG at a cut-off of 1.18pg/ml, the sensitivity and specificity were 0.94 and 0.82 respectively.

Conclusion: Vitreous GM and BDG above the indicated threshold level could suggest a fungal infection, even when cultures are negative.

14th

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