MANIPAL
ACADEMY of HIGHER EDUCATION
(Institution of Eminence Deemed to be University)

McGill | GLOBAL HEALTH PROGRAMS | PROGRAMMES DE SANTÉ MONDIALE

Contagion

The annual MAC ID Newsletter

Issue 4 – March, 2021

A publication by

Manipal Centre for Infectious Diseases (MAC ID)

Prasanna School of Public Health

Manipal Academy of Higher Education, Manipal

0820 2933505

macid.mu@manipal.edu

http://macid.manipal.edu/

Follow us on Manipal Center for Infectious Diseases @macidmahe

Team MAC ID

Team Members: MAHE

Dr Kavitha Saravu
Professor and Head
Dept. of Infectious Diseases, KMC, Manipal
MAC ID Coordinator, Manipal

Dr Shrikala Baliga
Deputy Director
Quality & Compliance, Mangaluru Campus
Professor
Dept. of Microbiology, KMC, Mangalore

Dr Chiranjay Mukhopadhyay
Associate Dean
KMC, Manipal
Professor
Dept. of Microbiology, KMC, Manipal

Dr Kiran Chawla
Professor
Dept. of Microbiology, KMC, Manipal

Dr John Ramapuram
Medical Superintendent, KMC, Mangalore
Professor
Dept. of Medicine, KMC, Mangalore

Dr Sneha Deepak Mallya
Associate Professor
Dept. of Community Medicine,
KMC, Manipal

Dr T S Murali
Associate Professor
Dept. of Biotechnology
Manipal School of Life Sciences, Manipal

Team Members: McGill University

Dr Charles P Larson
Interim Director
McGill University Global Health Programs
National Coordinator
Canadian Coalition for Global Health
Research, Canada

Dr Madhukar Pai
Director
Canada Research Chair in Epidemiology &
Global Health
Associate Director
McGill International TB Centre, Canada

Dr Nitika Pant Pai
Medical Scientist
The Research Institute of McGill University
Health Centre, Canada
Associate Professor of Medicine
McGill University Health Centre, Canada
Researcher, Division of Clinical Epidemiology,
McGill University Health Centre, Canada

Dr Michael Libman
Director
J D MacLean Center for Tropical Diseases,
Canada
Director, Tropical Diseases Clinic
McGill University Health Centre, Canada
Professor of Medicine
McGill University Health Centre, Canada

Dr Cedric Yansouni
Associate Director
J D MacLean Center for Tropical Diseases,
Canada
Assistant Professor
McGill University Health Centre, Canada

Dr Momar Ndao
Director
National Reference Center for Parasitology,
Canada
Associate Professor of Medicine
McGill University Health Centre, Canada

Dr Faiz Ahmad Khan
Director, TB Clinical Services, Montreal Chest
Institute
McGill University Health Centre, Canada
Respirologist
McGill University Health Centre, Canada
Assistant Professor of Medicine
McGill University Health Centre, Canada

CONTENTS

SECTION 1

Epistola...

The letters...

Editors' note

Dr. T. S. Murali
Department of Biotechnology
Manipal School of Life Sciences, Manipal

Dr. Pooja Rao
Department of Microbiology
Kasturba Medical College, Mangalore

Dear Friends

Historians in the future would look at the year 2020 and wonder what went wrong, how it went wrong and how the human civilization which could send men to Moon could not prevent or effectively control a global pandemic which killed millions of people. The Spanish Flu or the 1918 influenza pandemic, considered to be one of the deadliest pandemics faced by humans, infected one third of the world's population. However, it was a time when the World War I was still raging, microbiology as a field of science was still at its infancy, and there were no antiviral drugs or antibiotics to treat the infections. The current pandemic has completely banished the common misconception that industrialized countries have successfully eliminated all infectious diseases. The virus did not discriminate between a developed country and a third world country and the only countries that came out successful were those who followed strict hygiene and strong scientific principles. We can safely say that humankind is still not prepared to face the consequences of Nature not so in its quite benevolent mood and the way forward is to invest in scientific inventions with focus on research and innovation especially in neglected fields such as Infectious Diseases. It also gave an opportunity for all of us to appreciate and salute the wonderful sacrifice made by health care sectors and sanitary workers in demanding conditions day in and day out.

We have been fortunate to be in a safe setting and as the whole world limps back to its normal self, we bring to you the 4th edition of our Centre's newsletter 'Contagion'. As the old saying goes "Why reinvent the wheel, when things are going well", some excellent work from previous editors made our work wonderfully simple in designing the newsletter. This newsletter is a compilation of all the major events related to infectious diseases, including a snapshot of international conference held at Manipal and various other workshops organized at Manipal and Mangalore campuses. The wonderful lectures by eminent faculty from across the globe during these meetings not only motivated the budding researchers but also encouraged the organizers to create venues for such interactions. We have also brought together some interesting articles from members of MAC ID and take this opportunity to thank all the contributors.

MAC ID has supported young investigators to actively take up research and this is reflected in the number of applications for seed grant awards. Not only this provides a wonderful opportunity to kick start their research career, but also a platform to showcase their research acumen and attract international collaborations. We are highly confident that the seed grant awardees will go on to achieve higher accolades and receive bigger grants in the near future. It is also highly rewarding to note that MAC ID supports young and upcoming researchers to attend national and international conferences and present their findings which will provide them with wonderful exposure to interact with leaders in the field of infectious diseases. The list of publications with MAC ID affiliation has been increasing steadily and it is praiseworthy to note that within a short period of time since its inception, MAC ID has made short but steady strides as can be observed from the funding obtained by MAC ID members from international grant agencies.

We also have some interesting scientific and popular articles, case reports and other brain teasers from our members and we are highly hopeful that it will make for interesting reading. At this point, we should all thank the support and encouragement provided by MAHE in nurturing Manipal Centre for Infectious Diseases (MAC ID) and creating a separate Department for Infectious Diseases in Manipal. We thank once again all the contributors, Ms. Chethana from MAC ID for compiling all the articles, M/s. AdSyndicate for the wonderful art work and Dr. Kavitha Saravu, Dr. Madhukar Pai and the whole MAC ID team in reposing faith in us to be editors of this exciting newsletter. We sincerely hope that you cherish reading this newsletter and request you to provide your valuable feedback to make it more appealing, engaging and at the same time kindle your scientific spirit.

Au revoir!!!

Coordinators' Message

Dr. Kavitha Saravu
Coordinator MAC ID
MAHE, Manipal

The year 2019, the year of the COVID-19 pandemic, has been something which is unprecedented for our generation. The pandemic has changed the lives of all in ways which was hard to imagine. As the countries had to dig deep to manage the catastrophe, let alone control the pandemic, health care workers had to step up and hold the fort in their own capacity worldwide. Undoubtedly all our activities came to a standstill except the case management of sick and needy.

Soon we equipped ourselves, framed local guidelines and started informing other providers and the public about COVID-19 case management and infection control through virtual CME's, in-person visits to various hospitals in the District and through various media. Our members were in the forefront of COVID-19 case management; and some of us offered scientific inputs to the district administration when sought for the effective management of the situation.

Before the pandemic we had successfully hosted an international conference in August which had brought eminent Tropical Medicine and Infectious Diseases specialists from across the globe which inspired the attendees to aspire and to do more.

Our constant efforts in advancing Infectious Diseases practice, education and research over a decade and in the last 5 years through MACID along with able Leadership of MAHE and KMC resulted in establishment of the Department of Infectious Diseases at Kasturba Medical College, Manipal, a remarkable milestone in our journey.

While we value our strong collaborations with McGill University under the banner of Manipal McGill Program of Infectious Diseases, we have expanded our reach with other International Universities such as Mayo Clinic, USA, Charite University, Berlin, Heidelberg University, Germany, Yale University, USA and Wayne State University, USA to name a few. I commend Dr. T.S. Murali and Dr. Pooja Rao who have done an immaculate work in bringing out the newsletter 'Contagion' which highlights the events held, celebrates the achievements of our members and brings out the unique perspectives from our collaborators. I extend my thanks to the MACID Core Committee members for their inputs, and gratitude to MAHE Leadership for their guidance. I look forward to all members' active participation in MACID activities so that we benefit mutually and wish all the readers an interesting read of the 'Contagion'.

SECTION

2

Opus...

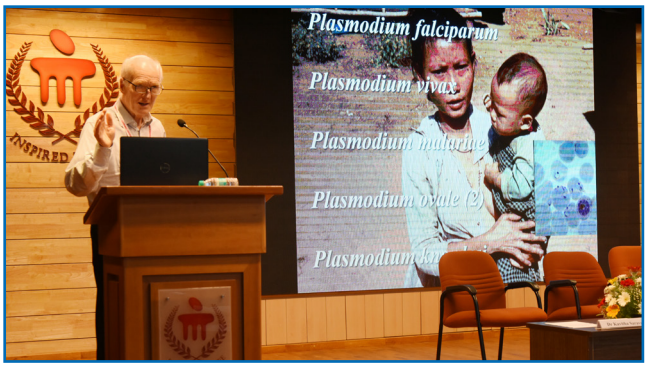
The work so far...

1 Events Organized by MAC ID

A) 3rd Manipal International Infectious Diseases Conference

10th and 11th August 2019

Inaguration of 3rd Manipal International Infectious Diseases Conference 2019
From Left to Right: Dr. Kavitha Saravu; Dr. Vinod Bhat; Dr. Sneha D Mallya; Dr. Poornima Baliga; Dr. Sharath Rao



Key Note Speaker:
Sir Nicholas J White,
Professor of Tropical Medicine
at Oxford and Thailand

The 3rd Manipal International Infectious Diseases Conference 2019, was organized on August 10th and 11th by Manipal Center for Infectious Diseases (MAC ID), Prasanna School of Public Health in association with the Department of Medicine, Kasturba Medical College, Manipal and McGill Global Health Program, Canada on the theme "Tropical Infections and Global Health". It brought together over 210 interested faculties, students and research scholars.

Dr. Sharath Rao, Dean, KMC, Manipal welcomed the gathering. Dr. Kavitha Saravu, the Coordinator of MAC ID gave the overview of activities of MAC ID and the conference. The Conference was inaugurated by the Vice Chancellor, Dr. Vinod Bhat and he envisioned that in coming days "One Health" approach and surveillance should be the way forward for early detection of infectious disease outbreaks. The guest of honor was Dr. Poornima Baliga, who released the MAC ID newsletter 'Contagion' and wished the best for the deliberations. Dr. Sneha Deepak Mallya, Associate Professor of Community Medicine, proposed the vote of thanks.

Sir Nicholas J White, Professor of Tropical Medicine at Oxford and Thailand, gave a key note on Malaria: The past, present and future. He traced the history of malaria, evolution of drug resistance in malaria. He hinted that the malaria vaccines could potentially be valuable in low endemic areas to eliminate malaria.

In another key note, Dr. Ravi Vasanthapuram, Professor of Neurovirology at NIMHANS, Bangalore, highlighted the epidemiology of Acute encephalitis syndrome, newer testing algorithms, and the need for early identification of treatable causes of encephalitis for improved outcomes.

Dr. David Richard Bell, Global Health Expert from Seattle, USA spoke on "Diagnostics of Acute fever: Technology Innovation meets reality" and spoke on challenges in availability and use of point of care diagnostics, biomarkers for disease severity and the importance of true costs of diagnostics for the national program. He also highlighted on the methods available for detection of low level malaria parasitemia in elimination settings.

Prof. Nicholas P J Day, Professor of Tropical Medicine at Oxford and Thailand gave an overview of antimicrobial resistance globally, need for better ways of estimates incorporating clinical outcomes and alluded to antibiotic footprints as communication tools. He also spoke on the iceberg phenomenon of melioidosis, and the high risk of diabetic patients acquiring the infection and the increasing need

for laboratories capable of identifying the bug responsible for melioidosis.

Dr. Jesse Papenberg, Paediatric Infectious diseases specialist from McGill University, Canada, spoke on Advanced Molecular Diagnostics/POC tests in Respiratory Infections and emphasized the need to choose the diagnostics wisely and the need for influenza vaccination. He emphasized that despite efforts to improve prevention and management in paediatric pneumonia, the burden remains huge. He suggested that determining the causative agent still presents a challenge at both individual and population level and antibiotics are being overused in paediatric CAP and bronchiolitis.

A talk titled "The Indian Scenario of HAI and AMR: Results from India AMR Surveillance Network" presented by Prof. Purva Mathur from AIIMS, New Delhi, highlighted the alarming rates of drug resistance. She spoke on the ICMR initiative on Antimicrobial Stewardship across Indian hospitals to curtail AMR.

Dr. Ram Gopalakrishnan, Infectious Diseases specialist from Apollo Hospitals, Chennai, discussed the Current Options and Strategies for the treatment of drug resistant Gram Negatives in India and infections in immunocompromised patients. Dr. Swati Rajagopal, Infectious Diseases and Travel Medicine Consultant from Bangalore, presented a talk on "Management of Drug Resistant Gram Positives". Dr. John Jude Prakash, Professor of Microbiology from Christian Medical College, Vellore, spoke on epidemiology and diagnosis of Scrub Typhus and other Rickettsiosis.

Dr. Patricia Fontela, Paediatric Intensivist from McGill University, Canada, discussed about the utility of biomarkers in reducing the duration of antibiotics. Dr. Reeta Mani, Additional Professor of Neurovirology from NIMHANS, Bangalore, presented the recent updates on antemortem diagnosis and management of Rabies and newer simplified vaccine schedule.

Dr. Manisha Madkaikar, Director of National Institute of Immunohaematology from KEM Hospital, Mumbai, spoke on Primary immunodeficiency in Children and adults. She also gave another talk on "Infection induced HLH". She highlighted that Infection induced HLH diagnosis requires a high index of suspicion and only 10 % of cases are familial. However, she emphasized that we must rule out familial HLH even in suspected secondary HLH cases.

On the 2nd day of the conference, there were several talks on disease outbreaks. Dr. Sajeeth Kumar, Medical Superintendent and Professor of Medicine, Kozhikode Medical College, spoke on the "Lessons learnt from Nipah virus outbreak in Kerala". Though it is a deadly infection, a strategic management plan and skilled team effort saved the day, he stressed. Dr. G. Arun Kumar, Director of Manipal Institute of Virology, gave a talk on Emerging Viral Hemorrhagic Diseases such as KFD, Ebola, Dengue haemorrhagic fever and Crimian Congo Haemorrhagic fever (CCHF). An interactive session on what to publish, how to publish and where to publish by Sir Nicholas Day, Prof. Nicholas White and Dr. David Bell was moderated by Dr. Sneha Deepak Mallya, KMC, Manipal and Dr. T.S. Murali from Manipal School of Life Sciences.

An informative panel discussion on "Outbreak management: The Road ahead" was led by Dr. Kavitha Saravu. Eminent panelists including Dr. Sajeeth Kumar, Dr. Shah Hossain, Dr. Chiranjay Mukhopadhyay and Dr. Arunkumar emphasized the need for surveillance in the community and the lab, need for more laboratories equipped with skills and technology to detect the pathogens, coordinated rapid response system and the need for strengthening of infection prevention practices.

The conference was attended by more than 200 delegates, from USA, Germany, Malaysia and within India from Delhi, Punjab, Gujarat, Maharashtra, Tamil Nadu, Andhra Pradesh, Kerala and Karnataka. They included practitioners, consultants, researchers, post graduates and faculty of various streams related to ID. There were more than 100 abstracts on various themes and they were of very good quality; top 14 were presented as oral presentations. An ID quiz was held for the post graduate student delegates by Dr. Suneel Mundkur, Professor of Paediatrics, KMC, Manipal, which was of high quality and was well appreciated.

The conference concluded with a valedictory function with Dr. Jesse Papenberg, Dr. Chiranjay Mukhopadhyay, and Dr. T.S. Murali awarding prizes to winners of various competitions. Dr. Kavitha Saravu, expressed gratitude to all who helped in organizing the conference and contributed to its success.

B) Guest lecture by Dr. Jesse Papenburg

12th August 2019

Dr. Jesse Papenburg, Paediatric Infectious Disease Specialist and Medical Microbiologist, McGill University Health Care Center, Canada

Team:
Department of Paediatrics,
KMC, Mangalore

Department of Paediatrics, KMC, Mangalore, in association with Manipal Center for Infectious Diseases, PSPH, MAHE, Manipal organized a guest lecture by Dr. Jesse Papenburg, Paediatric Infectious Disease Specialist and Medical Microbiologist, McGill University Health Care Center, Canada on 12th August 2019 at 3 pm to 4 pm in Sushrutha Hall, KMC Hospital Attavar, Mangalore. Dr. Jesse Papenburg lectured on the topic “Advanced Molecular diagnostics/POC tests in paediatric respiratory infections”. Faculty from Microbiology and Paediatrics Departments and trainees from Paediatrics Department attended the guest lecture. The session was very informative and interactive.

C) Guest lecture by Dr. Sheela Shenoi

12th August 2019

Dr. Sheela Shenoi, Assistant Professor of Medicine, Yale School of Medicine, USA

Left to Right: Dr. Sheela Shenoi, Dr. H Manjunatha Hande and Dr. Kavitha Saravu

A full house of experts in HIV and TB research together with postgraduate students in the field assembled for a Guest lecture, held at Shirdi Saibaba Hall Manipal, organized by Manipal Centre for Infectious Diseases (MAC ID), Prasanna School of Public Health, MAHE, Manipal, in association with Departments of Medicine and Infectious Diseases, KMC, Manipal on 29th October 2019.

The lecture was presented by Prof. Sheela Shenoi, Assistant Professor of Medicine, Yale School of Medicine, New Haven. The talk was on "TB Preventive Therapy and Contribution to TB Elimination".

Chemoprophylaxis against tuberculosis is necessary for protection against the disease, especially in high risk and vulnerable population (in patients living with HIV and in children less than 5 years of age). The traditional practice was to administer Isoniazid prophylactic therapy (IPT) to PL-HIV and under 5 contacts of TB patients for a period of 6 months.

Dr. Shenoi spoke about alternate chemoprophylaxis regimens – of shorter duration which have been found non-inferior to the standard protocol. They include, 3 months of weekly Isoniazid with Rifapentine, 1 month of daily INH and Rifapentine, 4 months of daily Rifampicin. Longer duration of INH has been found to be similarly effective in preventing TB, but with lesser compliance and risk of higher toxicity. There is no substantial increase in the risk of INH resistance secondary to IPT and the benefits outweigh the risks.

D) Symposium on HIV and Inauguration of Department of Infectious Diseases

4th November 2019

Dr. Zelalem Temesgen,
Director of HIV Program,
Director of Mayo Clinic Center for Tuberculosis,
Mayo Clinic
USA

Standing: left to right: Dr. Krishnananda Prabhu; Dr. Anil Bhat; Dr. Nitin Gupta; Dr. Muralidhar Varma; Dr. Kavitha Saravu; Dr. Vasudeva Acharya
Sitting: left to right: Dr. Sharath Kumar; Dr. Vinod Bhat; Dr. Zelalem Temesgen; Dr. Poornima Baliga; Dr. Raviraja V Acharya

A half day Symposium on HIV was held on 4th November 2019 organized by Manipal Center for Infectious Diseases (MAC ID) in association with Departments of Medicine and Infectious Diseases, which hosted 90 faculty members, students and research scholars. CME speakers, Dr. Nitin Gupta (Assistant Professor, Department of Infectious Diseases, KMC, Manipal) spoke on Initiation of ART in PLHIV in India and Dr. Zelalem Temesgen (Infectious Diseases Specialist, Mayo Clinic, USA) highlighted on Tuberculosis in the setting of HIV. This was followed by a Case discussion on HIV by Dr. Zelalem Temesgen and Dr. Kavitha Saravu.

Department of Infectious Diseases was inaugurated by the chief guest Dr. Zelalem Temesgen. Pro Vice Chancellor, MAHE Manipal, Dr. Poornima Baliga remarked that, “The beginning of this department will educate medical students. We are also aiming to start many other departments like this which in turn will benefit the society.” The function was presided by Dr. Vinod Bhat, who in his address said, “The time when the general practitioner treated every disease has gone. Now, all the specialties and specialists are needed for treatment of the disease. This is not just the demand of the medical sciences, but it is also the wishes of people. Though it is a division of internal medicine, this department will help in treating infectious disease in better way”. Dr. Sharath Rao, Dean, KMC, Manipal welcomed the gathering. The session was concluded with vote of thanks by Dr. Muralidhar Varma, Associate Professor, Department of Infectious Diseases, KMC, Manipal.

E) Symposium on HIV – KMC, Mangalore

5th November 2019

Inauguration of Symposium on HIV
Left to Right: Dr. Nutan Kamath, Dr. John Ramapuram, Dr. Zelalem Temesgen

Left to Right:
Dr. Zelalem Temesgen,
Dr. Nutan Kamath

A symposium was held at KMC Attavar on 5th November 2019. The event was inaugurated by Dr. Nutan Kamath, Associate Dean, KMC, Mangalore and Dr. Zelalem Temesgen, Infectious Diseases specialist, Mayo Clinic, USA. The symposium was organized by Department of Medicine, KMC, Mangalore and Manipal Center for Infectious Diseases.

Dr. John Ramaparum delivered a talk on HIV care at KMC Attavar. Dr. Zelalem Temesgen gave an invited lecture on TB in the setting of HIV. Dr. Deepak Madi presented interesting ID cases from KMC, Mangalore. Post graduates from Department of Medicine presented challenging HIV cases in clinical practice. The postgraduate session was moderated by Dr. Deepak and Dr. Basavaprabhu. Around 92 delegates from various departments attended the symposium.

F) Symposium on Infectious Diseases outbreaks

25th January 2020

A group photo from Symposium on Infectious Diseases outbreaks

Dr. Ian Cropley, Infectious Diseases specialist from Royal Free hospital, London

With the global concerns growing over the novel coronavirus (2019-nCoV) epidemic outbreak in China and its spread worldwide, Department of Infectious Diseases at KMC, Manipal in association with Manipal Centre for Infectious Diseases, organized a timely and relevant symposium on Infectious Diseases outbreaks on 25th January 2020. The symposium discussed the efficient Public Health system intervention in various epidemic outbreaks around the world.

Dr. Shah Hossain, Public Health Specialist from Prasanna School of Public Health, MAHE, highlighted the importance of various public health measures including quarantine and surveillance measures undertaken in India during outbreaks of cholera, Avian flu, H1N1 and CCHF. He emphasized on the need of "surveillance measures to be on alert" as every year presents with a major epidemic outbreak.

Dr. Ian Cropley, Infectious Diseases specialist from Royal Free hospital, London, discussed the public health measures undertaken in the UK during the Ebola outbreak. He opined that optimization of care was the key factor in reducing mortality. He reflected his experience with epidemic management with well-practiced plans supported by both public and financial support. He also highlighted the poor international response and unavailability of research studies on the go which to an extent led to inability to ascertain best possible treatment. He stressed on multi-agency co-operation, rapid development of therapeutics, the need to work in partnerships with affected countries and more importantly the importance of a "plan to activate response team at short notice" to efficiently manage epidemics.

Dr. Ankur Rakesh, from Médecins Sans Frontières (MSF), coordinator for Global Health and Humanitarian Medicine - South Asia, discussed the various public health interventions during the Yemen cholera outbreak. He threw light on the various challenges faced by clinicians in providing basic healthcare in a civil war struck country like Yemen.

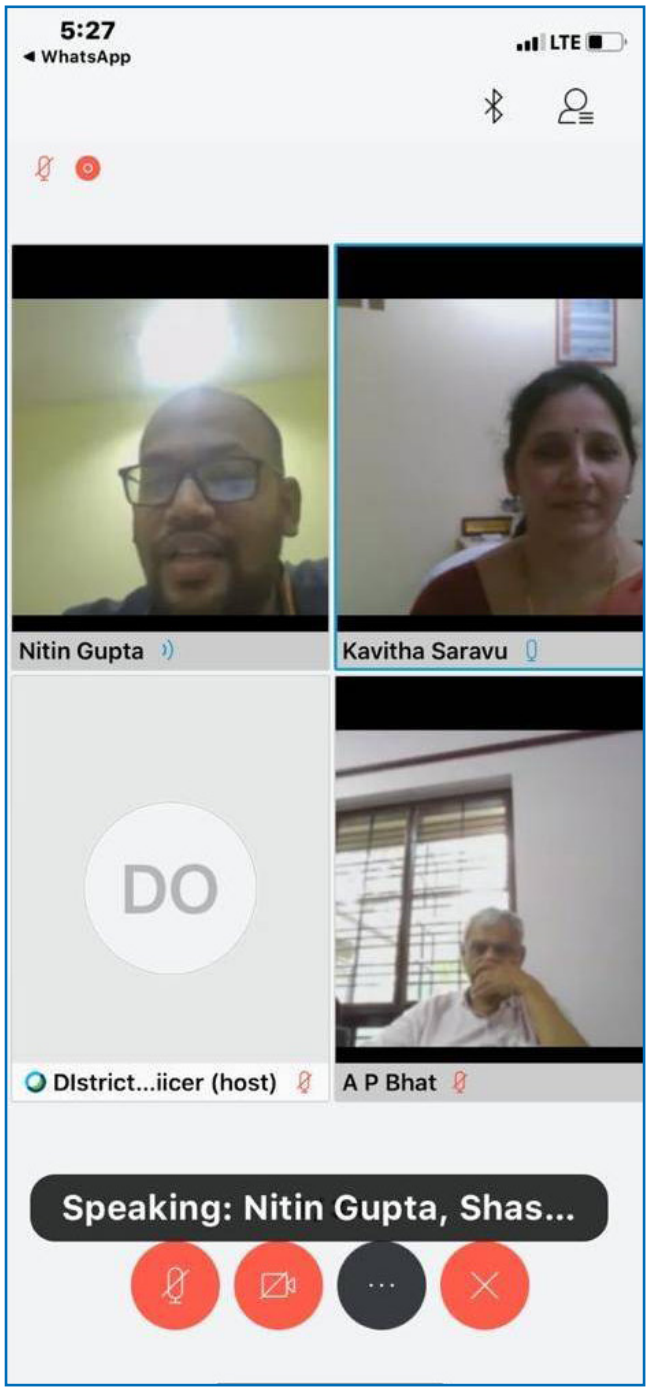
Apart from the invited lectures, the symposium also provided an opportunity for the audience to discuss their queries on the novel coronavirus outbreak with Dr. Arunkumar, Director of Manipal Institute of Virology. He confirmed the laboratory preparedness for the detection of novel emerging pathogens in India.

The symposium was attended by 103 delegates including public health officials from Karwar and Udupi and faculties, students and research scholars of MAHE. Dr. Kavitha Saravu, Professor and HOD, Department of Infectious Diseases, KMC, Manipal, hosted the sessions, while Dr. Nitin Gupta, Assistant Professor, Department of Infectious Diseases, KMC, Manipal coordinated the events.

The increasingly complex picture of infectious diseases outbreaks all over the world was highlighted by the lengthy discussions during the symposium. The session stressed on promoting improved public health through communication and outreach with the outreach extending to policymakers. The symposium was highly successful and added significantly to the knowledge base of this important topic.

G) Webinar series on COVID-19

17th and 25th July, 2020



A Webinar series on COVID-19
Top: Dr. Nitin Gupta, Dr. Kavitha Saravu

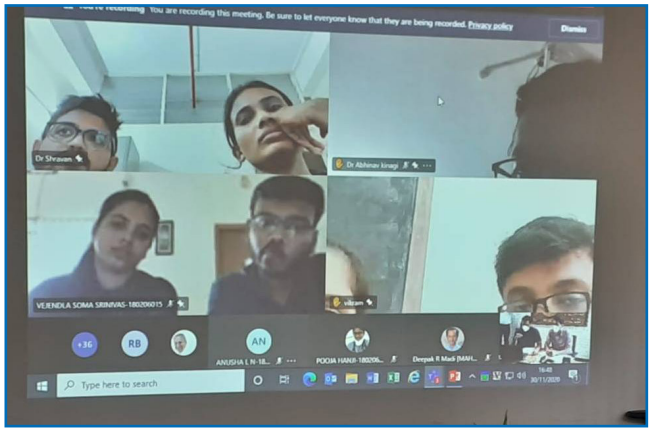
A Webinar series on COVID-19 was held on 17th and 25th July, 2020. It was organized by Department of Infectious Diseases, KMC, Manipal, Manipal Center for Infectious Diseases (MAC ID), PSPH, MAHE, Manipal, in association with District Health and Family Welfare Services, Udupi. Dr. Prashanth Bhat, Nodal officer COVID-19, Udupi District, moderated the webinar series 1 held on 17th July, 2020 and Dr. Kavitha Saravu, Professor and Head, Department of Infectious Diseases, KMC, Manipal and Dr. Chidananda Sanju, District Tuberculosis Officer, Udupi, moderated webinar series 2 held on 25th July, 2020. Around 235 delegates participated in the webinar across Udupi district, Karnataka and other parts of India on 17th July and 160 delegates on 25th July.

In webinar series-1, Dr. Shashikiran Umakanth, Medical Superintendent and Nodal officer COVID-19, Dr. TMA Pai Hospital, Udupi, spoke about "COVID -19 Epidemiology in India with Special Reference to Udupi". Dr. Nitin Gupta, Assistant Professor, Department of Infectious Diseases, KMC, Manipal, spoke about Clinical features and Diagnosis. Dr. Kavitha Saravu, Professor and Head, Dept. of Infectious Diseases, KMC, Manipal and Coordinator, Manipal Center for Infectious Diseases (MAC ID), Manipal, spoke about Pharmacological Management in COVID-19.

In webinar series-2, Dr. Vishal Shanbhag, Assistant Professor, Department of Critical Care Medicine, KMC, MAHE, Manipal, spoke about Critical Care Management, stressing the use of High Flow Nasal Cannula (HFNC). Dr. Muralidhar Varma, Associate Professor, Department of Infectious Diseases and Chair Person of HICC, KMC, MAHE, Manipal, spoke about Antimicrobial Stewardship and Infection Control in the times of COVID-19. Dr. Gagandeep Kang, Professor, The Wellcome Trust Research Laboratory, Division of Gastrointestinal Sciences, Christian Medical College, Vellore, gave a bird's eye view about "Vaccines and Future Aspects of COVID 19".

H) HIV Update 2020 – KMC, Mangalore

30th November 2020



Participants of HIV quiz competition

Organizers of HIV quiz competition

HIV update 2020 was organized by the Department of Medicine, KMC, Mangalore and Manipal Center for Infectious Diseases on 30th November 2020 as a part of World AIDS day. Dr. John Ramapuram, Professor and Medical Superintendent, Kasturba Medical College, Mangalore was the organizing Chairperson and Dr. Deepak R Madi, Associate Professor, Department of Medicine, KMC, Mangalore and Dr. Basavaprabhu, Associate Professor, Department of Medicine, KMC, Mangalore were the organizing secretaries.

The conference was attended by more than 60 delegate participants comprising of faculty, students and research scholars from different institutions.

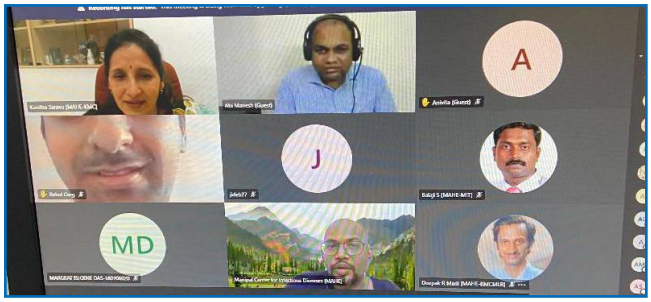
Dr. Sathish Rao (Additional Professor, Department of Medicine, KMC, Mangalore) spoke about “How do I choose ART in practice”. Dr. Farhan Fazal (Assistant Professor, Department of Medicine, KMC, Mangalore) highlighted on “How do I manage ART resistance”.

Dr. Shafir Kassim (Assistant Professor, Department of Medicine, KMC, Mangalore) addressed about “How do I manage CNS infections in PLHIV”, and Dr. Basavaprabhu, (Associate Professor, Department of Medicine, KMC, Mangalore) discussed “Interesting cases on HIV”.

HIV quiz was conducted by Dr. Nikhil Victor D’Souza, Senior Resident, Department of Medicine, KMC, Mangalore. Four medical colleges from Mangalore participated in this quiz competition. KMC, Mangalore bagged the first place.

I) Virtual World AIDS Day Symposium

1st December 2020



Participants and resourse person of Virtual World AIDS Day Symposium

Lt. Gen. (Dr.) M. D. Venkatesh, Vice Chancellor, MAHE Manipal, addressing the inaguration

On the eve of World AIDS Day 2020, with the theme "Global Solidarity, Shared Responsibility" multiple programs were organized/co-hosted by the Manipal Center for Infectious Diseases.

E-poster competition and video making competition was organized by MAC ID and Manipal College of Nursing, Manipal for Students of MAHE. While E- poster competition was on the theme "Global Solidarity, Shared Responsibility", the theme for video making competition was "The Rights of Women and Girls". Dr. Linu Sara George coordinated these two competitions.

Quiz competition was organized by MAC ID, Departments of Community Medicine, and Infectious Diseases, KMC, Manipal for under graduate and postgraduate students of MAHE and other Colleges from India. Dr. Sneha Mallya and Dr. Shashidhar V were the quiz masters.

In connection with the World AIDS Day, Manipal Center for Infectious Diseases and Department of Infectious Diseases, KMC, Manipal organized Virtual World AIDS Day symposium 2020 on 1st December 2020.

Dr. Kavitha Saravu, Professor & Head, Department of Infectious Diseases and co-ordinator MAC ID gave the welcome address and overview of the symposium. The symposium was inaugurated by the Chief Guest – Lt. Gen. (Dr.) M. D. Venkatesh, Vice Chancellor, MAHE Manipal. Dr. Sharath Rao, Dean, KMC, Manipal and the guest of honor, announced the results of various competitions held in connection with the World AIDS Day. Dr. Nitin Gupta, Assistant Professor, Department of Infectious Diseases at KMC, Manipal and Organizing Secretary of the symposium delivered the vote of thanks.

The symposium was attended by 79 participants comprising of faculty, students and research scholars from India and overseas.

Dr. Animesh Ray (Assistant Professor, Department of Medicine, All India Institute of Medical Sciences, New Delhi) spoke about Pulmonary Manifestation in HIV. Dr. Priscilla Rupali (Professor, Department of Infectious Diseases, Christian Medical College, Vellore) highlighted on Immune Reconstitution Inflammatory Syndrome (IRIS).

Dr. Raghavendra Rao, (Professor & Head, Department of Dermatology, Kasturba Medical College, Manipal) discussed about Sexually Transmitted Infections (STIs) in HIV, and Dr. Abi Manesh, Associate Physician, Grade–II, Department of Infectious Diseases, Christian Medical College, Vellore addressed about CNS Manifestations in HIV. Dr. Nitin Gupta, (Assistant Professor, Department of Infectious Diseases, KMC, Manipal) gave a talk on How to Design ART Regimen in Indian Context.

International Faculty, Dr. Sheela Shenoi, (Assistant Professor of Medicine, Medical Director, Connecticut AIDS Education and Training Center, Yale School of Medicine, USA) spoke about Care of Patients Living with HIV During the Times of COVID-19, and Dr. Aakriti Pandita, (Assistant Professor, Department of Infectious Disease, University of Colorado Hospital (UCH), Aurora, Colorado) gave a thought provoking lecture on Care of TB Patients During the times of COVID-19.

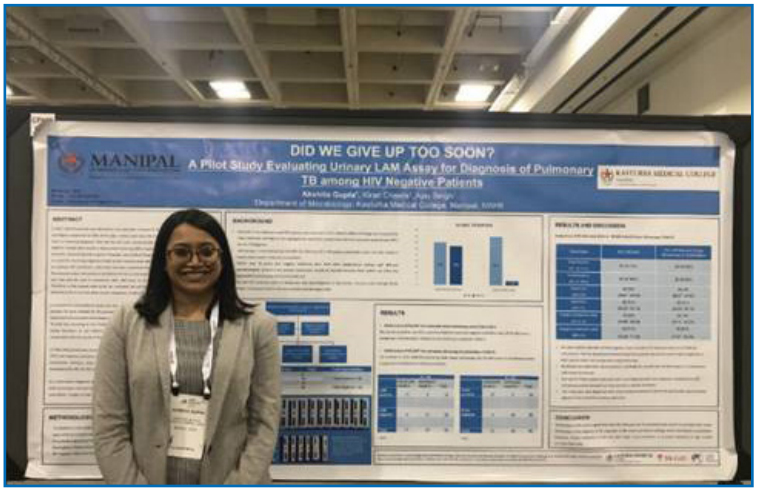
2 Seed Grants Awarded - 2020-21

Awardee's Name and Department		Title of the project
Dr. Nitin Gupta Assistant Professor, Dept. of Infectious Diseases, KMC, Manipal		Impact of Rapid diagnostic tests in patients with acute febrile illness presenting to a tertiary care hospital in South India: an open diagnostic intervention randomized controlled trial
Dr. Bharath Raja Guru Professor, Dept. of Biotechnology, MIT, Manipal		Implant and nano-formulation of acyclovir and prodrug of acyclovir using biodegradable polymers to treat Herpes Simplex virus infections
Dr. Kanav Khera Assistant Professor, Dept. of Pharmacy Practice, MCOPS, Manipal		Genotypic profiling and docking studies using gyrA gene obtained from Fluoroquinolone-resistant urinary isolates of E. coli
Dr. Suchitra Shenoy Associate Professor, Dept. of Microbiology, KMC, Mangalore		Nanoparticle-encapsulated antibiotics to combat bacterial biofilm
Dr. Barnini Banerjee Associate Professor, Dept. of Microbiology, KMC, Manipal		Molecular epidemiology of the methicillin resistant *Staphylococcus aureus* and their association with biofilm formation in patients with bone and joint infection

3 Student Travel Awards

Ms. Akshita Gupta

Post graduate,
Department of Microbiology,
KMC, Manipal



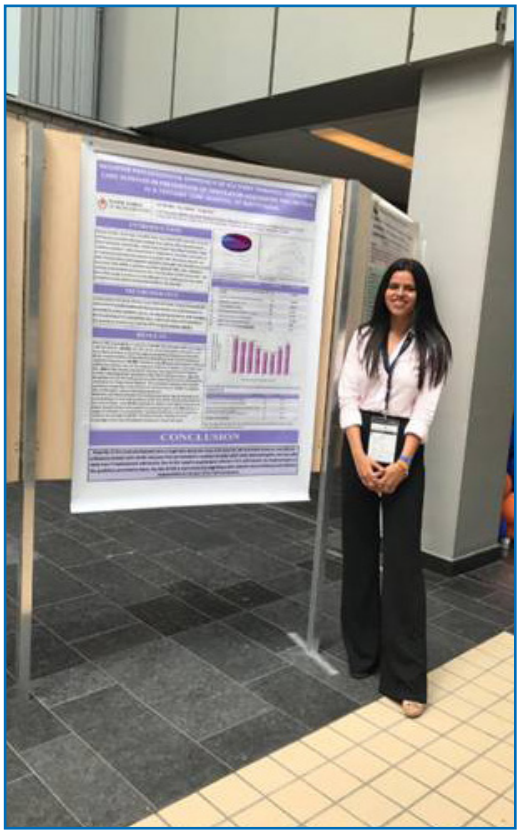
Guided by Dr. Kiran Chawla, Professor and Head, Department of Microbiology, KMC, Manipal

Title: Did we give up too soon? A pilot study on evaluation of urinary LAMP assay for diagnosis of Pulmonary TB among HIV negative patients

Poster Presentation at American Society of Microbiology, held at Moscone Center, San Francisco from 20th–24th June, 2019

Ms. Fiza Jakhar

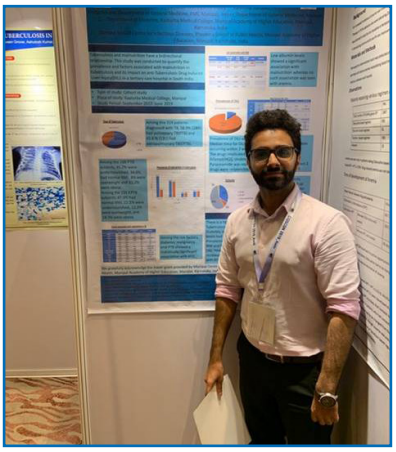
Under Graduate,
Final year MBBS, KMC, Mangalore



Guided by Dr. Pooja Rao, Associate Professor, Department of Microbiology, KMC, Mangalore

Title: Negative psychological approach of ICU staff towards ventilator care bundles in prevention of ventilator-associated pneumonia in a tertiary care hospital of South India

Poster Presentation at University Medical Center of Groningen, held at Groningen, Netherlands from 3rd–7th June, 2019



Mr. Nihal Ali

Post graduate,
Department of Medicine, KMC,
Manipal

Guided by Dr. Kavitha Saravu, Professor and Head, Department of Infectious Diseases, KMC, Manipal

Title: Prevalence of malnutrition in tuberculosis patients in an Indian tertiary care Centre: a descriptive analysis

Poster Presentation at Clinical Infectious Diseases Society (CIDSCON), held at Kochi, Kerala from 23rd–25th August, 2019

Mr. Dattatreya Sitaram

Post graduate,
Department of Orthopedics,
KMC, Manipal

Guided by Dr. Shyamasunder Bhat N, Professor and Head, Department of Orthopedics, KMC, Manipal

Title: Clinical profile and role of investigation modalities in patients with *Brucella spondylodiscitis*

Oral Presentation at Canara Orthopedics Society, Spine Chapter of Karnataka Orthopedic Association, held at Mangalore from 27th–29th September, 2019

Mr. Tushar Shaw

Ph.D. Student,
Department of Microbiology,
KMC, Manipal

Guided by Dr. Chiranjay Mukhopadhyay, Associate Dean, KMC, Manipal and Professor, Department of Microbiology, KMC, Manipal

Title: Determining the influence of environment factors on the presence of *B. pseudomallei* in the Indian soil.

Oral Presentation at Institute of Microbiology and Biotechnology, Vietnam National University, Hanoi held at Sheraton Hotel, Hanoi, Vietnam from 14th–15th October, 2019

SECTION 3

Novus...

What's New in ID...

1 Articles by McGill Faculty

It's time to use Covid-19 innovations and systems to reimagine TB care

Dr. Madhukar Pai
Canada Research Chair in Epidemiology & Global Health and Associate Director, McGill International TB Centre, McGill University, Montreal, Canada

Even as the world comes to grips with the mounting death toll due to the Covid-19 pandemic, the WHO released its 2020 Global Tuberculosis Report last week. The news is not good. Nearly 1.4 million people died from TB in 2019. Of the estimated 10 million people who developed TB that year, some 3 million were either not diagnosed, or were not officially reported to national authorities.

As expected, the Covid-19 pandemic is making things worse, with 25-30% drops in TB notifications reported in 3 high burden countries – India, Indonesia, the Philippines – between January and June 2020 compared to the same 6-month period in 2019. These reductions in case notifications and ongoing disruptions to TB services could substantially increase TB deaths.

As I previously wrote, together, Covid-19 and TB pose a deadly, dual threat - a syndemic. Tremendous catch-up work, advocacy, and funding is needed, to get back on track, even as the pandemic is pushing millions of people into extreme poverty. That cannot be good for TB, since Poverty and TB are old pals.

In the early days of the pandemic, there was optimism that TB technologies and systems could help end the Covid-19 pandemic. Indeed, molecular technologies widely used for TB are being used to test for Covid-19, and the BCG vaccine for TB is being tested for Covid-19. National TB program staff (e.g. contact tracers) are engaged in the Covid-19 response. TB wards have been re-purposed to serve as Covid-19 wards.

But now, given the massive setback to progress in reaching any of the TB targets, it's time for the TB community to ask: are there Covid-19 innovations and systems that can be effectively leveraged to reimagine TB care?

"In many low- and middle-income countries, TB programs became the foundation of an effective early response to Covid-19. Now, as we are urgently rebuilding disrupted core health services for TB and other conditions, we have an opportunity to draw on the toolbox of innovations that have been created for Covid-19," said Catharina Boehme, CEO of FIND, Geneva.

By speaking with a large number of experts, I could indeed identify several opportunities for the TB field (and vice-versa).

Education, risk assessment & screening

Mobile apps & services (e.g. using Whatsapp & chatbots) are being widely used for public education on Covid-19, for risk or self assessment, screening and linkage to testing, for contact tracing and mapping.

For example, South Africa, building on its success with MomConnect, has reached over 7 million people using a suite of digital tools (e.g. COVID-19 HealthAlert & COVID-19 HealthCheck). India's open-source Aarogya Setu mobile app has been downloaded by over 150 million individuals. If these apps can enhance TB contact tracing, that would be a huge advance, since contact investigation is an effective but underused intervention in many high TB burden countries.

According to Zameer Brey, a Senior Program Officer at the Bill & Melinda Gates Foundation in South Africa, these platforms and technologies are being

repurposed for TB. "The 'disruptive' innovations that emerged during the Covid-19 pandemic were waiting beneath the surface to really enhance patient-centered care across the most vulnerable communities. The biggest tragedy would be to quickly bury those innovations and bury the hope of a more patient centric system," he said.

Another way to screen for TB and Covid-19 is to use digital chest x-rays (highly portable systems now exist), with artificial-intelligence (AI) solutions to make the interpretation easier and less reliant on expert radiologists. Such AI-based solutions already exist, for TB as well as Covid-19. AI-based algorithms can also identify CT scans with COVID-19 associated pneumonia.

"While TB needed AI interventions, the development of such technologies was slow because TB was (and still is) a poor person's disease. Covid-19 has not only ushered more adoption for existing AI interventions, but forced us to think what we can build beyond usual offerings," said Prashant Warier, CEO of Qure.ai. "Initially, while a lot of TB solutions were repurposed for Covid-19, now there is an opportunity to reverse-purpose several Covid-19 solutions for TB," he added.

Automated recognition of cough duration and sound patterns might help encourage care-seeking and potentially screen for conditions such as TB and Covid-19. Indeed, innovative R&D around this is happening (e.g. Hyfe cough tracker app). "How could the ability to detect and classify coughs not be transformational?" asked Peter Small, a TB expert and innovator at Global Health Labs.

Raghu Dharmaraju, a VP at Wadhwani AI is hopeful about cough-based screening as well as greater use of data science for pandemic response. "My deepest hope is that we use this crisis to accelerate the shift to truly data-driven health systems," he said.

Innovative sample collection and diagnosis

"Innovative community-based (decentralized) testing and enhanced case finding can be lessons learned from Covid-19 and scaled up for TB," said Antonio Flores, a HIV/TB specialist with Médecins Sans Frontières.

Puneet Dewan, a physician and TB expert with Global Health Labs agrees. "There has never been so much enthusiasm and money in diagnostic testing," he says. He hopes some good can come out of the current crisis. "We have to ensure we end up with products and systems that meet TB control needs," he said.

The demand for rapid and simpler Covid-19 testing has pushed companies and health systems to innovate around what samples to collect, where to collect them, and how to make testing easier to access. For example, samples such as saliva, rinse and gargle, oral swabs, and even sampling of face masks are being actively tried out. Better and cheaper swabs have been developed (e.g. polyester-based Q-tip-type swab).

Tremendous effort is being made to develop home-based, self-tests for Covid-19. Mobile testing sites, drive-through testing, and sample collection via community health workers, neighborhood pharmacies, schools and workplaces are all happening.

Currently, TB testing is highly reliant on sputum, a sample that is not easy to collect and process. TB testing is also not easily accessible at the primary care level. So, if some of the innovative approaches around Covid-19 sample collection & near-patient access can be applied to TB, this might help reduce the massive diagnostic gap in TB.

"The unprecedented speed with which Covid-19 tests have been developed is proof that even technically challenging diagnostics can become reality in record time," says Morten Ruhwald, Head of TB at FIND, Geneva. He believes there is huge potential to expand Covid-19 technologies across a spectrum of respiratory diseases.

There are several rapid molecular diagnostic platforms that are currently running Covid-19 and TB tests. Some of them are designed for point-of-care use (e.g. GeneXpert and TrueNat), while others are meant for high-throughput, centralized laboratories (e.g. BD Max, Abbott m2000, Roche Cobas). Wider use of molecular technologies and bi-directional testing can only be good for TB, and help the field get rid of suboptimal tools such as smear microscopy.

In addition, great progress has been made with rapid, point-of-care antigen testing for Covid-19. Adapting this to develop simpler POC tests for TB would be a massive advance. Rapid, high-sensitivity urine LAM antigen detection technology holds great promise

and will benefit from all the technology development around Covid-19 rapid testing.

"Simple self-sampling (e.g. from face masks) appears within reach – and in combination with cutting-edge molecular detection assays like CRISPR, this could make at-home diagnosis of respiratory infections not just as straightforward as a pregnancy test, but as accurate as conventional diagnostic methods," said Morten Ruhwald.

"I am very enthusiastic about the possibility of porting true point-of-care, non-sputum based diagnostic systems for use in TB. It's not just the instrumented platforms, but non-instrumented disposables that have taken a flying leap forward," said Puneet Dewan.

Innovations in care delivery

"Remote service provision has come to stay due to Covid-19," said Ifeanyi Nsofor, CEO of EpiAFRIC and Director of Policy and Advocacy at Nigeria Health Watch. And everyone now sees the value of care close to home (primary care).

Indeed, because of lock-downs and physical distancing requirements, tremendous advances have been made in the area of tele-health, online consultations, house calls by doctors, use of call centers, e-pharmacies, use of digital adherence technologies (e.g. smart pillboxes, video observed therapy), and home delivery of medicines using health workers, ride-sharing services, etc. All of these can and should be leveraged for TB, at a larger scale than what is currently happening.

"Covid-19 is providing a huge boost to the at-home delivery market for medicines," said Prashant Yadav, a supply chain expert and professor at INSEAD. "The infrastructure that many privately funded startups & social enterprises are creating could be extremely useful for TB patients especially if sometime in the future we transition to even shorter treatment regimens which can be self-administered with a tele-consult follow-ups," he added.

Indeed, we now have hopes for a 1 month treatment for latent TB infection, a 4-month treatment for active TB, and a 6-month oral treatment for drug-resistant TB. If these can be combined with tele-consults and at-home delivery of medicines, it could revolutionize TB care.

According to Yadav, Covid-19 has created a sudden and growing interest in improving healthcare supply chains. "Many of the initiatives are focusing on resolving system bottlenecks in procurement, distribution and supply chain information systems. These will go a long way in ensuring healthy supply chains for all medicines," he said.

Better data, data visibility and usage

Most TB programs still rely on annual reports and paper-based reporting systems that are no longer fit for purpose. Covid-19 shows us the power of real-time data aggregation, analysis and usage.

During this pandemic, an astounding number of real-time Covid-19 trackers, vulnerability indices, geospatial mapping tools and dashboards have been launched, often by collaborative networks of scientists and citizens. This has provided real-time data for public health and personal use. Rapid data sharing has also provided early epidemiological and clinical insights. Most countries are conducting rapid prevalence and infection surveys, to enhance routine surveillance. Covid-19 has also accelerated the use of electronic medical records.

TB has never seen this level of investment in data systems. Lack of good data has always blunted effective TB response and made it harder to ensure accountability.

"Investments on data systems and tools like vulnerability indices are key to deploying a more precise response (for Covid-19 or TB)," says Sema Sgaier, Director of Surgo Foundation. "Vulnerability indices can be powerful predictive tools that enable policy makers to identify geographies that will have the hardest time to mitigate the health, social, and economic impacts of a disease like TB, and guide policy makers to the types of mitigation interventions they should be betting on," she added. Machine learning and big data can also help precisely target those who need extra support.

Infection control & behavior change

Despite being an airborne respiratory infection with high risk of occupational transmission, TB infection control has received little attention in high-burden countries. Covid-19 shows that healthcare systems can find ways to protect healthcare workers and

people can change their behaviors to reduce risk, for themselves and others.

"The overlooked story is how human behavior change can interrupt transmission. A no holds barred attack on how we change behavior should be essential response to this pandemic and TB," said Peter Small.

Routine use of personal protection equipment by healthcare workers, large-scale use of face masks by the public, better triaging and cohorting within health facilities, safer disposal of respiratory secretions, and advances in research into aerosols & airborne transmission (and engineering controls) can all help interrupt TB as well as Covid-19 transmission.

Because of Covid-19, the use of face masks has become less stigmatized, and there is wider acceptance that anyone can get a respiratory infection. Hopefully, this will make TB less stigmatized.

Social safety

Covid-19 has taught the world about the importance of social safety nets that include paid sick leave, unemployment benefits, direct cash transfers, food supplements, and a heightened focus on social determinants. Greater education of the public and community engagement is also evident in many settings. And public health investment is now clearly understood as a 'social good.'

Since TB is primarily a disease of poverty and is highly correlated with social determinants such as malnutrition and poor housing, such social security benefits must be more widely available to all persons with TB, especially in low- and middle-income countries. A purely biomedical approach to TB is unlikely to succeed. In the same vein, greater engagement of communities most affected by TB is critical for success.

Public-private partnerships for care delivery

During this crisis, governments across the world have found a variety of mechanisms (e.g. price caps, strategic purchasing of services, better regulation) to tap into the private health sector for Covid-19 testing and treatment. As noted by WHO, many LMICs have a large and growing contingent of private sector health service delivery actors that have historically been weakly governed and poorly coordinated. "Now more than ever LMICs need a whole-of-government and whole-of-society approach as they immerse in the battle against COVID-19."

A recent survey showed wide variations in the cost of Covid-19 testing in the private health sector across LMICs. However, some countries have successfully made Covid-19 testing more affordable and accessible via private laboratories. Similar private-provider initiatives are also underway for TB, and deserve to be taken to scale, since the private health sector is a major source of TB care in several high TB burden countries.

Global partnerships & collaborative research

The pandemic has transformed medical research and publishing. We now have rapid access to information via pre-prints and open access publications. Most medical and scientific conferences are now free and easily accessible to people around the world.

There are many open data data platforms to foster research collaborations and R&D. "Despite TB being the biggest infectious diseases burden, and especially affecting LMICs, many publications are still sitting behind a paywall," laments Muge Cevik, a clinical lecturer in infectious diseases at the University of St Andrews.

The pandemic has also inspired several multilateral global collaborations and partnerships (e.g. ACT Accelerator, COVAX), pooling of funding for new tool development & delivery, patent pools to increase access, and other approaches to increase access to new tools.

Such partnerships are urgently needed for TB, where slow access to new tools is a long-standing concern. 'We have demonstrated that with global solidarity, a lot can be achieved in a short time. Open data, open access research and (to some extent) pooling of technology have all become the norm and should be continued for global threats like TB," said Soumya Swaminathan, Chief Scientist at WHO.

Rapid, multi-centric trials & evaluation studies (e.g. Solidarity trial, Recovery trial), faster regulatory approval processes, greater cohesion among scientists for evidence-driven interventions (e.g. John Snow Memorandum), and multi-sectoral responses within and across countries have all been noticeable during this crisis. "Wouldn't it be great to

see the same concerted efforts to develop TB drugs and tests as we've seen for Covid-19?" asked Antonio Flores.

Muge Cevik would like TB researchers to be more open to adaptive clinical trial designs. "It seems like we are constantly stuck in long phase 3 studies of single drugs," she lamented.

Jennifer Furin, a TB physician and advocate, laments that TB has received almost no attention compared to Covid-19, despite the fact that TB kills millions of people each year. "Research predicts a gloom-and-doom scenario for TB as a result of Covid-19, but if we are smart, persistent, and creative in adapting some of Covid-19's successes, this could actually become our finest hour," she argued. Along with her colleagues, she has listed potential collateral benefits from the Covid-19 pandemic to TB and HIV services.

Aakriti Pandita, an infectious diseases physician at the University of Colorado has survived both Covid-19 and TB. "Covid-19 is unclogging many novel pathways towards medical advancement that otherwise would have taken a lifetime to develop. In fact, in time, Covid-19 may actually prove to be one giant leap in medical science and global health if we use it to our advantage," she said.

Beyond disease silos

While the Covid-19 crisis has brought a great deal of attention to health, it is unclear whether such interest will sustain when the crisis dies out. Will Covid-19 create more disease silos, or will we finally see stronger health systems that can offer better primary healthcare? Will countries continue to invest in public health?

Daksha Shah, Deputy Executive Health Officer for the Municipal Corporation of Greater Mumbai in India has coordinated services for both TB and Covid-19. "Right now, the health system is most receptive (she highlighted the "My Family, My Responsibility" campaign in her state as an example) and we should build on this for improving care for TB, non-communicable diseases, and other conditions," she said.

Grania Brigden, Director of the TB Department at The Union agrees. "I, personally, do not want to see another vertical disease program established with separate funding streams/donors/multinational organizations," she said. "I think there is a benefit to thinking how/if TB integrates with the Covid-19 response and in high burden contexts becomes the cornerstone of a comprehensive approach to lung health," she added. Since Covid-19 has put the spotlight on the importance of comorbidities, she hopes a similar attention will be paid to addressing comorbidities that often accompany TB (e.g. HIV, diabetes, malnutrition).

Yogan Pillay, country director of CHAI in South Africa, sees great potential for leveraging Covid-19 innovations for TB. The problem, he said, is "none of these are new to the TB community. How to get everyone to take TB seriously as they are with Covid-19?", he asked.

Jennifer Furin has similar concerns. "The dazzling list of innovations for Covid-19 only happened because wealthy nations are just as at risk of Covid-19 as poor nations," she said. "So we need to be fierce advocates to make sure these tools for Covid-19 are applied to TB because rich countries have revealed themselves for what they are: self-interested to the core," she added.

Jennifer Furin is right - the billions of dollars invested in Covid-19 vaccines is orders of magnitude higher than the investments made in TB vaccine development since the dawn of humankind. We might have Covid-19 vaccines within a year, but will still be using a 100-year old vaccine for TB next year.

Saurabh Rane, a drug-resistant TB survivor and advocate has a compelling message. "I don't want to know why the world didn't respond this way for TB when it kills over a million people every year. But now that we are building tools to fight Covid-19, I beg everyone to use them to fight TB as well," he said. I agree wholeheartedly with him. There cannot be a more opportune moment for the TB community to leverage Covid-19 innovations to reimagine TB care, and make universal health coverage a reality.

Reproduced from:

https://www.forbes.com/sites/madhukarpai/2020/10/22/time-to-tap-covid-19-innovations--systems-to-reimagine-tb-care/?sh=2b82b2da494d

2 Articles from MAHE faculty

Point-of-care Ultrasound (POCUS) for Improved Diagnosis of Tuberculosis

Lisa Ruby[1], Stefan Weber[2], Claudia Denkinger[3], Sabine Bélard[4], Kavitha Saravu[5]

[1] Medical Student, Charité University Berlin, Department of Pediatric Pneumology and Immunology, Charité – University Hospital Berlin, Berlin, Germany

[2] MD, Department of Tropical Medicine, Heidelberg University Clinics, Heidelberg, Germany

[3] MD, Department of Tropical Medicine, Heidelberg University Clinics, Heidelberg, Germany

[4] MD, PhD, MSc, DTM&H (London), Department of Pediatric Pneumology and Immunology, Charité – University Hospital Berlin and Berlin Institute of Health, Berlin, Germany

[5] MD, DNB, DTM&H (London), Professor & Head, Department of Infectious Diseases, Kasturba Medical College, Manipal, India

Tuberculosis continues to cause immense global morbidity and mortality [1,2]. The majority of tuberculosis patients suffer from pulmonary tuberculosis (PTB), a form of tuberculosis where the disease is limited to lung parenchyma. In a considerable proportion of tuberculosis patients the disease spreads beyond the lungs, leading to extra-pulmonary tuberculosis (EPTB) which can virtually affect any organ. The risk of tuberculosis is increased in individuals with impaired immunity (e.g. young pediatric, elderly, HIV-infected or diabetic patients) with HIV being the most important risk factor for EPTB and diabetes a widespread risk factor for PTB. Some patients present with both PTB and EPTB, called concurrent PTB and EPTB.

Advances in TB diagnostic tests (e.g. GeneXpert, lipoarabinomannan urine testing) have improved diagnosis of tuberculosis [3]. However, in around a third of tuberculosis patients confirmation of tuberculosis is not achieved and therefore diagnosed on clinical grounds. Imaging plays a crucial diagnostic role in the diagnostic work-up for tuberculosis, with CXR being the standard imaging tool for PTB [4].

Point-of-care ultrasound has become a quick and cost-efficient tool for focused sonographic examinations by the treating physician that impact on immediate patient management decisions [5]. Point-of-care ultrasound applications have been established in many different medical fields, including infectious diseases, and with technological advances portable ultrasound devices become affordable bedside imaging devices. Focused Assessment with Sonography for HIV-associated Tuberculosis (FASH) has become a well-established POCUS application in low-and middle-income countries which bear a high burden of tuberculosis and HIV. The FASH protocol focused on EPTB comprises assessment of free fluid in the pericardial, pleural and abdominal cavity (tuberculous effusions), hepatic or splenic hypo-echoic focal lesions (tuberculous micro-abscesses), and abdominal lymphadenopathy (tuberculous lymphadenitis) [6] – all sonographic features of common manifestations of EPTB. In South Africa, in adults (mostly HIV-infected) with presumptive (and subsequently confirmed) EPTB or disseminated TB, sonographic abdominal lymphadenopathy, pericardial effusion, ascites, or splenic lesions were highly predictive of active TB [7].

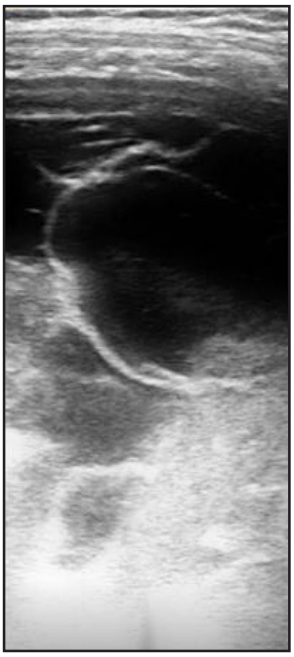


Figure 1
Tuberculous pleural effusion

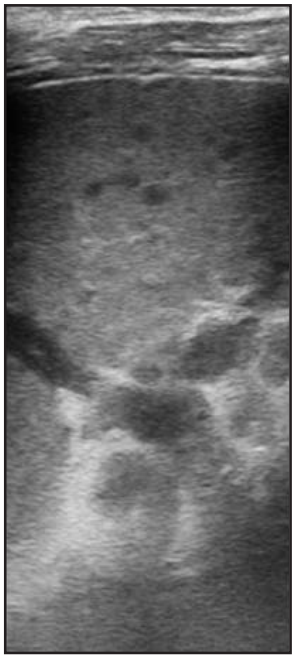


Figure 2
Tuberculous splenic micro-abscesses and lymphadenopathy in a TB/HIV co-infected patient

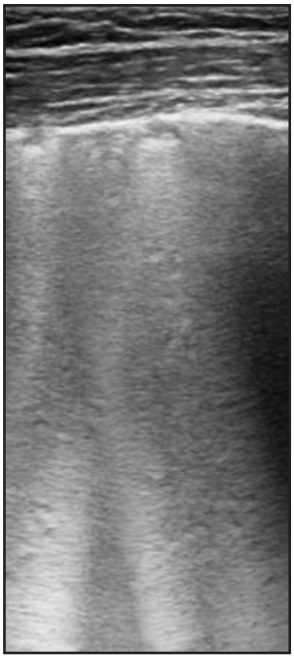


Figure 3
Lung ultrasound in a patient with miliary TB

Figure 4
Bedside lung ultrasound on a tablet based device

A first project of the Indo-German research collaboration on tuberculosis evaluated POCUS for EPTB in presumptive adult tuberculosis patients in Manipal in 2016 [8]. Presumptive TB patients prospectively underwent POCUS evaluating for pericardial, pleural and ascitic effusion, abdominal lymphadenopathy, and hepatic and splenic microabscesses. Findings were correlated with TB category (confirmed TB, clinical TB, unlikely TB), HIV status, and discharge diagnoses. A total of 425 patients underwent POCUS; 20% were HIV-positive. POCUS findings were more common in HIV/TB co-infected patients than in HIV-positive patients with unlikely TB (60% versus 22%, $p < 0.001$). Abdominal lymphadenopathy and splenic microabscesses were strongly associated with TB in HIV-positive patients ($p = 0.002$ and $p = 0.001$). POCUS increased the detection of patients with concurrent PTB and EPTB by 15% to a total of 26%. POCUS findings did not correlate with TB in HIV-negative patients; a third of HIV-negative patients with unlikely TB and POCUS findings had cancer, another third other infectious diseases. In conclusion, sonographic findings were common in HIV-positive and HIV-negative presumptive TB patients. POCUS was a useful bedside test for the detection of HIV-associated EPTB. In HIV-negative patients, POCUS detected features associated with EPTB but also of malignancy and other infectious diseases.

Lung ultrasound (LUS) is an established tool in critically ill patients [9]. The utility of LUS for the diagnosis of ARDS has previously been studied in Manipal [10] and a high test accuracy of LUS for pneumonia has been reported by many studies and meta-analyses for pediatric and adult patients [11-13]. LUS also showed potential to differentiate bacterial from viral etiology of community-acquired pneumonia in children [14] and to identify PTB [15]. Lower respiratory tract infections (LRTI) including tuberculosis, pneumonia and HIV-associated respiratory infections still pose a major health concern in India and novel approaches are urgently needed to reduce morbidity and mortality. Diagnostic value of extended point-of-care LUS (LUS extended to the examination of focused ultrasound for pericardial effusion, abdominal lymphadenopathy and splenic micro-abscesses) for differentiating between bacterial, viral, fungal pneumonia and tuberculosis in HIV-uninfected and HIV-infected adults is yet to be explored.

The role of POCUS in routine TB diagnosis has yet to be defined and diagnostic algorithms are still lacking a substantiated pool of evidence for the accuracy of ultrasound for any given TB entity. A Cochrane review has concluded, that studies with robust reference standard are scarce [16] and evidence on promising sonographic lung findings possibly suggestive of PTB are so far rather anecdotal [17, 18]. Moreover, data on POCUS as a potential follow-up tool appears promising, however more data is needed to inform guidelines [19]. In future, we therefore aim to further strengthen the evidence on POCUS for TB (both PTB and EPTB) with a prospective, longitudinal and blinded cohort study including a robust reference standard.

References

[1] Paulson T. 2013. Epidemiology: A mortal foe. Nature. 502(7470):S2-3.

[2] Cambau E, Drancourt M. 2014. Steps towards the discovery of *Mycobacterium tuberculosis* by Robert Koch, 1882. Clin Microbiol Infect. 20(3):196-201.

[3] Stevens WS, Scott L, Noble L, Gous N, Dheda K. 2017. Impact of the GeneXpert MTB/RIF Technology on Tuberculosis Control. Microbiol Spectr. 5(1).

[4] Pedrazzoli D, Lalli M, Boccia D, Houben R, Kranzer K. 2017. Can tuberculosis patients in resource-constrained settings afford chest radiography? Eur Respir J. 49(3).

[5] Bornemann P, Jayasekera N, Bergman K. 2018. Coming soon to primary care? The Journal of Family Practice. 67(2).

[6] Heller T, Wallrauch C, Goblirsch S, Brunetti E. 2012. Focused assessment with sonography for HIV-associated tuberculosis (FASH): a short protocol and a pictorial review. Crit Ultrasound J. 4(1):21.

[7] Patel MN, Beningfield S, Burch V. 2011. Abdominal and pericardial ultrasound in suspected extrapulmonary or disseminated tuberculosis. South African Medical Journal 101(1):39-42.

[8] Weber SF, Saravu K, Heller T, Kadavigere R, Vishwanath S, Gehring S, et al. 2018. Point-of-Care Ultrasound for Extrapulmonary Tuberculosis in India: A Prospective Cohort Study in HIV-Positive and HIV-Negative Presumptive Tuberculosis Patients. Am J Trop Med Hyg. 98(1):266-73.

[9] Lichtenstein DA. 2015. BLUE-protocol and FALLS-protocol: two applications of lung ultrasound in the critically ill. Chest. 147(6):1659-70.

[10] Sanjan A, Krishnan SV, Abraham SV, Palatty BU. 2019. Utility of Point-of-Care Lung Ultrasound for Initial Assessment of Acute Respiratory Distress Syndrome Patients in the Emergency Department. J Emerg Trauma Shock. 12(4):248-53.

[11] Ye X, Xiao H, Chen B, Zhang S. 2015. Accuracy of Lung Ultrasonography versus Chest Radiography for the Diagnosis of Adult Community-Acquired Pneumonia: Review of the Literature and Meta-Analysis. PLoS One. 10(6):e0130066.

[12] Heuvelings CC, Bélard S, Familusi MA, Spijker R, Grobusch MP, Zar HJ. 2019. Chest ultrasound for the diagnosis of paediatric pulmonary diseases: a systematic review and meta-analysis of diagnostic test accuracy. Br Med Bull. 129(1):35-51.

[13] Chavez MA, Shams N, Ellington LE, Naithani N, Gilman RH, Steinhoff MC, et al. 2014. Lung ultrasound for the diagnosis of pneumonia in adults: a systematic review and meta-analysis. Respiratory Research.15(1):1-9.

[14] Berce V, Tomazin M, Gorenjak M, Berce T, Lovrenčič B. 2019. The usefulness of lung ultrasound for the aetiological diagnosis of community-acquired pneumonia in children. Scientific Reports. 9(1):1-10.

[15] Agostinis P, Copetti R, Lapini L, Badona Monteiro G, N'Deque A, Baritussio A. 2017. Chest ultrasound findings in pulmonary tuberculosis. Trop Doct. 47(4):320-8.

[16] Van Hoving DJ, Griesel R, Meintjes G, Takwoingi Y, Maartens G, Ochodo EA. 2019. Abdominal ultrasound for diagnosing abdominal tuberculosis or disseminated tuberculosis with abdominal involvement in HIV-positive individuals. Cochrane Database of Systematic Reviews. 2019(9).

[17] Heuvelings CC, Bélard S, Janssen S, Wallrauch C, Grobusch MP, Brunetti E, et al. 2016. Chest ultrasonography in patients with HIV: a case series and review of the literature. Infection. 44(1):1-10.

[18] Hunter L, Bélard S, Janssen S, van Hoving D, Heller T. 2016. Miliary tuberculosis: sonographic pattern in chest ultrasound. Infection. 44(2):243-6.

[19] Heller T, Wallrauch C, Brunetti E, Giordani M. 2014. Changes of FASH ultrasound findings in TB-HIV patients during anti-tuberculosis treatment. The International Journal of Tuberculosis and Lung Disease. 18(7):837-9.

Correlation of clinical severity and laboratory parameters with various serotypes in Dengue virus - A hospital based study

Pooja Rao[1], Basavaprabhu A[2], Suchitra Shenoy[3], Nikhil D`souza[4], Sridevi H B[5], Vaman Kulkarni[6]

[1,3]Department of Microbiology

[2,4]Department of Internal Medicine

[5]Department of Pathology

[6]Department of Community Medicine, Mangalore, Manipal Academy of Higher Education, Manipal, Karnataka, India

ABSTRACT

Objectives

Dengue fever being hyper-endemic with analogous presentations as in many other acute febrile illness, poses a challenge in diagnosis during the acute stage. Additionally, the coexistence of multiple serotypes further complicates the disease prognosis. The study was undertaken to determine the dengue virus serotypes, clinical and laboratory markers as predictors in the severity of infection.

Methods

A prospective study was conducted among 106 patients admitted with acute febrile illness having positive NS1 Antigen/ IgM ELISA. Clinical data was extracted from medical records including demographics, presence of comorbid conditions, clinical presentation, laboratory investigations, course including length of hospital stay and outcome. Detection of dengue serotypes was done by multiplex reverse transcriptase polymerase chain reaction (RT-PCR).

Results

Out of 106 RT PCR confirmed cases, DENV-3 was the most common serotype found in 56 (52.8%) patients, followed by DENV-3 and DENV-4 co-infection in 27 (25.4%) patients. Co-infection with more than one serotypes was witnessed in our study. Raised Liver enzymes and increased ferritin are good biomarkers in differentiating dengue from severe dengue with cut off levels for AST (134U/L), ALT (88U/L) and ferritin (3670 ng/ml). Musculoskeletal, followed by gastrointestinal manifestations were comparatively higher than respiratory, and cutaneous manifestations.

Conclusion

This study provides more information on the dengue serotypes. The clinical spectrum of dengue along with laboratory investigations ferritin, liver enzymes, platelet which could be used as potential biomarkers in prediction of severity. The data demonstrated will be useful in early detection and monitoring the disease.

Link: https://www.hindawi.com/journals/ijmicro/2020/6658445

SARS-CoV-2: A primer on the detection and vaccines

Apoorva Jnana*, Anjali Warrier*, Murali TS

Department of Biotechnology,
Manipal School of Life Sciences,
Manipal Academy of Higher Education, Manipal

* - Equal contribution by these two authors

Humankind is currently at a global pause enforced by a 50-200nm respiratory virus, Severe Acute Respiratory Syndrome Coronavirus – 2, that has claimed more than 1.7 million lives and infected 80 million individuals worldwide [1]. Several variables of the coronavirus disease (COVID-19) such as the full spectrum of host immune responses, varied clinical symptoms of disease and rates of viral transmission/ mutation are yet to be uncovered [2]. While social distancing and transmission mitigation strategies have helped us to keep the virus at bay, a return to pre-pandemic "normalcy" requires advances in detection technologies and effective vaccination programmes [3].

The current detection technologies are nucleic acid based methods (detection of viral RNA) and immunoassays (detection of anti-SARS-CoV-2 immunoglobulins). Nucleic acid based methods include Reverse transcription-polymerase chain reaction (RT-PCR) method [4], Reverse transcription loop mediated isothermal amplification [5], Recombinase Polymerase amplification [6] and next generation sequencing methods [7,8]. Of these, the most widely used method is RT-PCR, that amplifies the genetic material of SARS-CoV-2 to detect the virus and quantify the viral load and is the frontline diagnostic test for COVID-19 [4]. The targets for COVID-19 detection so far include regions in the envelope (E) gene, RNA dependent RNA polymerase (RdRP) gene, Nucleocapsid (N) gene, Spike protein (S) gene, and ORF1ab gene [1,4], of which E gene targeting is reported to have the highest sensitivity [4]. The estimated detection limit of the COVID-19 RT-PCR test is <10 copies/reaction which allows the detection of low viral titers at an early stage with 95% testing sensitivity [9]. However, RT-PCR is an expensive test requiring skilled technicians and expensive instruments [10]. Hence, these are often preceded by rapid, inexpensive serological tests such as Enzyme-linked immunosorbent assays (ELISAs) and Lateral Flow Immunoassays (LFIA). ELISA measures the host humoral immune response including IgM, IgG, and IgA to define previous exposure to the virus [11], and has a more than 80% accuracy in patients at a stage as early as 3 days from the development of the early symptoms [12]. LFIA allows rapid qualitative detection of the virus by measuring the SARS-CoV-2 antibodies or antigens using a portable diagnostic strip in ~15 min [13]. Together, these detection methods help in timely diagnosis of COVID19 patients allowing for effective antiviral therapies and control of the disease.

An important aspect of pandemic preparedness is prevention and control of the virus. As of December 14, 2020, 187 vaccine candidates have been reported, of which 62 are in human trials [14,15]. The vaccination strategies include inactivated and live, attenuated version of the coronavirus, viral like particles (they resemble the virus but lack the genetic material to replicate themselves), protein subunits (majority of the vaccines in development target the spike protein on the viral envelope), recombinant vectors (immunogenic parts of coronavirus are expressed on a replicating/non-replicating non-pathogenic virus such as adenovirus) and nucleic acid vaccines (introduction of genetic material such as DNA or RNA that encodes for pathogenic antigens) [16] (Fig 1, Table 1). Majority of the vaccines currently in development

are targeted towards the structural protein of coronavirus, S protein, a key protein involved in host attachment and subsequent pathogenicity [17,18]. Moderna and Pfizer (mRNA based vaccines) are currently approved for prevention of COVID-19 [19]. Early clinical trials have shown mRNA-1273 (Moderna vaccine candidate) to be well tolerated with no severe adverse effects in a population self identified as “white”, “Asian American”, “Hispanic” and “black” [20].

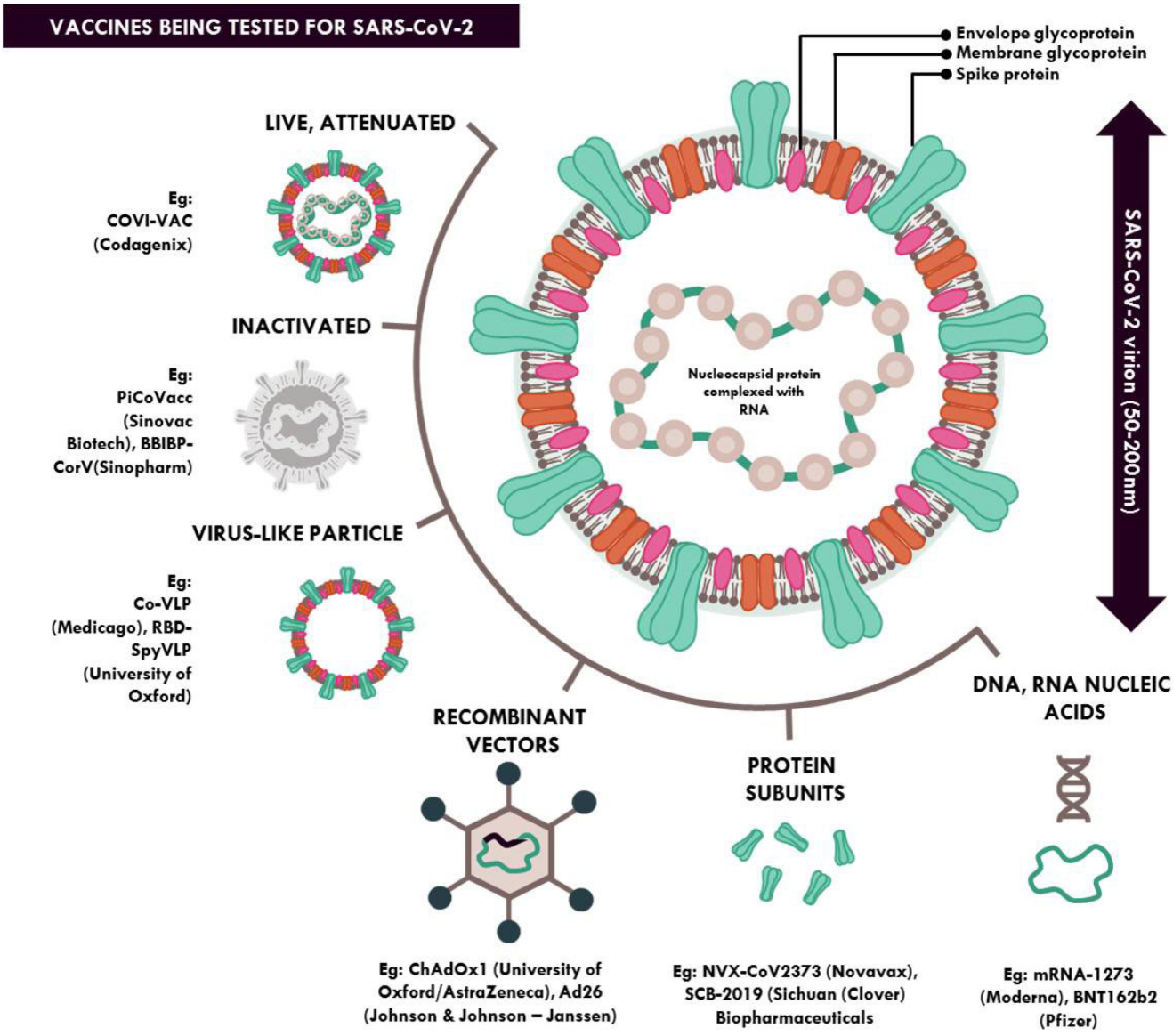


Figure 1: Schematic diagram illustrating SARS-CoV-2 virion and vaccines currently in pre-clinical/clinical trials. Adapted from [16, 21-23]. SARS-CoV-2 - Severe Acute Respiratory Syndrome Coronavirus 2, VLP - Viral like Particle, RBD – Receptor Binding Domain

Table 1: Vaccine strategies currently in development for COVID19 disease prevention

Platform	Vaccine Name	Developers	Target	Stage	Cost
Live virus	COVI-VAC	Codagenix	Whole virus	Phase I	NA
Inactivated virus	PiCoVacc	Sinovac Biotech	Whole virus	Phase III	NA
Inactivated virus	BBIBP-CorV	Sinopharm	Whole virus	Phase III	NA
VLP	Co-VLP	Medicago	Spike	Phase II	NA
VLP	RBD-SpyVLP	University of Oxford	Spike	Phase I	NA
Recombinant vector	ChAdOx1	University of Oxford/ Astra Zeneca	Spike	Phase III	500 INR (unconfirmed)
Recombinant vector	Ad26	Johnson & Johnson - Janssen	Spike	Phase III	NA
Protein subunit	NVX-CoV2373	Novavax	Spike	Phase III	NA
Protein subunit	SCB-2019	Sichuan (Clover) Biopharmaceuticals	Spike	Phase I	NA
DNA	INO-4800	Inovio pharmaceuticals	Spike	Phase I	NA
DNA	bacTRL-Spike	Symvivo corporation	Spike	Phase I	NA
RNA	mRNA-1273	**Moderna**	Spike	Phase III	$25 - $37
RNA	BNT162	**BioNTech SE/Pfizer**	Spike	Phase III	$19.50 for the first 100 million doses

Source: [3,16,24-26]

Note: Vaccines mentioned in bold are vaccines recommended by Center for Disease Control and Prevention for prevention of COVID-19. VLP – Virus Like Particle, NA – not available.

Pandemic preparedness involves development of an efficient vaccine that can be stored, easily scaled up for large scale manufacturing, be ready for trials and emergency authorization if and when any outbreak occurs [25]. The current speed of vaccine development for the SARS-CoV-2 virus does not reflect any omitted safety checks, but is rather a product of streamlining of logistic proceedings and efficient use of years of previous research on other coronaviruses such as Middle East Respiratory Syndrome virus [27]. While the promise of returning to pre-pandemic "normalcy" is tempting, it remains inconclusive considering that we have very limited data on the stability of these vaccines during distribution and long-term effects of the fast-tracked vaccines. However, it is comforting to know that should another wave of pandemic strike, the world would be better equipped to handle the crisis.

References

[1] World Health Organization. 2020. Diagnostic testing for SARS-CoV-2. Retrieved from https://www.who.int/publications/i/item/diagnostic-testing-for-sars-cov-2

[2] Perlman S. 2020. Another decade, another coronavirus. New England Journal of Medicine 382:760-762

[3] Jeyanathan M, Afkhami S, Smaill F, Miller MS, Lichty BD, Xing Z. 2020. Immunological considerations for COVID-19 vaccine strategies. Nature Reviews Immunology 20:615-632.

[4] Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DKW, Bleicker T, Brünink S, Schneider J, Schmidt ML, Mulders DG. 2020. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro Surveillance 25:2000045

[5] Yan C, Cui J, Huang L, Du B, Chen L, Xue G, Li S, Zhang W, Zhao L, Sun Y, Yao H. 2020. Rapid and visual detection of 2019 novel coronavirus (SARS-CoV-2) by a reverse transcription loop-mediated isothermal amplification assay. Clinical Microbiology and Infection 26:773–779

[6] Behrmann O, Bachmann I, Spiegel M, Schramm M, Abd El Wahed A, Dobler G, Dame G, Hufert FT. 2020. Rapid detection of SARS-CoV-2 by low volume real-time single tube reverse transcription recombinase polymerase amplification using an exo probe with an internally linked quencher (exo-IQ). Clinical Chemistry 66:1047-1054

[7] Holland LA, Kaelin EA, Maqsood R, Estifanos B, Wu LI, Varsani A, Halden RU, Hogue BG, Scotch M, Lim ES. 2020. An 81 nucleotide deletion in SARS-CoV-2 ORF7a identified from sentinel surveillance in Arizona (Jan-Mar 2020). Journal of Virology[Epub ahead of print].

[8] Korber B, Fischer WM, Gnanakaran G, Yoon H, Theiler J, Abfalterer W, Foley B, Giorgi EE, Bhattacharya T, Parker MD, Partridge DG. 2020. Spike mutation pipeline reveals the emergence of a more transmissible form of SARS-CoV-2. Cell 182:812-827

[9] Chu DKW, Pan Y, Cheng SMS, Hui KPY, Krishnan P, Liu Y, Ng DY, Wan CK, Yang P, Wang Q, Peiris M. 2020. Molecular diagnosis of a novel coronavirus (2019-nCoV) causing an outbreak of pneumonia. Clinical Chemistry 66:549–555

[10] Carter LJ, Garner LV, Smoot JW, Li Y, Zhou Q, Saveson CJ, Sasso JM, Gregg AC, Soares DJ, Beskid TR, Jervey SR. 2020. Assay techniques and test development for COVID-19 diagnosis. ACS Central Science 6:591-605

[11] Okba MMN, Muller MA, Li W, Wang C, GeurtsvanKessel CH, Corman VM, Lamers MM, Sikkema RS, de Bruin E, Chandler FD, Yazdanpanah Y. 2020. SARS-CoV-2 specific antibody responses in COVID-19 patients. Emerging Infectious Diseases 26:1478-1488

[12] Liu W, Liu L, Kou G, Zheng Y, Ding Y, Ni W, Wang Q, Tan Li, Wu W, Tang S, Xiong Z, Zheng S. 2020. Evaluation of Nucleocapsid and Spike Protein-based ELISAs for detecting antibodies against SARS-CoV-2. Journal of Clinical Microbiology 58:e00461-20

[13] D'Cruz RJ, Currier AW, Sampson VB. 2020. Laboratory Testing Methods for Novel Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2). Frontiers in Cell and Developmental Biology 8:468.

[14] Biorender COviD-19 vaccine and therapeutics tracker. 2020. COviD-19 vaccine and therapeutics tracker. Retrieved from https://biorender.com/covid-vaccine-tracker/

[15] Hu B, Guo H, Zhou P, Shi ZL. 2020. Characteristics of SARS-CoV-2 and COVID-19. Nature Reviews Microbiology 6:1-4

[16] Dai L, Gao GF. 2020. Viral targets for vaccines against COVID-19. Nature Reviews Immunology 18:1-10

[17] Padhi AK, Tripathi T. 2020. Can SARS-CoV-2 Accumulate Mutations in the S-Protein to Increase Pathogenicity? ACS Pharmacology & Translational Science 3:1023-1026

[18] Shin MD, Shukla S, Chung YH, Beiss V, Chan SK, Ortega-Rivera OA, Wirth DM, Chen A, Sack M, Pokorski JK, Steinmetz NF. 2020. COVID-19 vaccine development and a potential nanomaterial path forward. Nature Nanotechnology 15:646-655

[19] CDC. 2020. Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Persons for Coronavirus Disease 2019 (COVID-19). Retrieved from https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html

[20] Mahase E. 2020. Covid-19: Moderna vaccine is nearly 95% effective, trial involving high risk and elderly people shows. British Medical Journal 371.

[21] Holmes KV. 2003. SARS-associated coronavirus. New England Journal of Medicine 348:1948-1951

[22] Tregoning JS, Brown ES, Cheeseman HM, Flight KE, Higham SL, Lemm NM, Pierce BF, Stirling DC, Wang Z, Pollock KM. 2020. Vaccines for COVID-19. Clinical & Experimental Immunology 202:162-192

[23] V'kovski P, Kratzel A, Steiner S, Stalder H, Thiel V. 2020. Coronavirus biology and replication: implications for SARS-CoV-2. Nature Reviews Microbiology 28:1-6

[24] Funk CD, Laferrière C, & Ardakani A. 2020. A snapshot of the global race for vaccines targeting SARS-CoV-2 and the COVID-19 pandemic. Frontiers in Pharmacology 11:937.

[25] Lurie N, Saville M, Hatchett R, Halton J. 2020. Developing Covid-19 vaccines at pandemic speed. New England Journal of Medicine 382:1969-73.

[26] BuisnessToday.in. 2020. Coronavirus vaccine: list of top candidates, storage, price; all you need to know. Retrieved from https://www.buissnesstoday.in

[27] Ball P. 2020. The lightning-fast quest for COVID vaccines — and what it means for other diseases. Nature News Feature Retrieved from https://www.nature.com/articles/d41586-020-03626-1

Tuberculosis: Through the Artist's eye

Dr. Cynthia Amrutha Sukumar
Assistant Professor
Department of Medicine
KMC, Manipal

Have you ever tried reading someone's face and wondering what kind of person he is? Or looked at someone and judged his personality? The art of analyzing facial expressions traces its way back into history. From early caricatures on cave walls to Renaissance art, human expression and facial features have captivated artists across the globe. Leonardo Da Vinci was one such artist known for his fascination for human expression and human anatomy [1]. His eye for detail, while painting human visage is evident in his many works including the famed MonaLisa. Such was his discipline that he would be anatomically accurate in his paintings even at the cost of the art looking ugly or grotesque.

This brings us to the discussion of his famous sketch, "The Five Grotesque heads". Dating back to the 15th century, this work details a man (labelled 1 in the picture) surrounded by four ugly men (labelled 2, 3, 4 and 5 in the picture). The ugly men are painted with extreme features and expression [2]. These expressions were initially thought to depict human behaviour and personality, but later they were interpreted to depict human pathology, namely orofacial manifestations of tuberculosis [3]. Da Vinci was known to make detailed sketches of unique looking people around Florence. Back in the 15th century, when tuberculosis was largely an unknown disease, afflicted individuals were treated as outcasts. It is possible that this sketch depicts a man being robbed by four old men with tuberculosis.

Tuberculosis finds its origin over 150 million years ago when studies from bone samples from human settlement in the Mediterranean indicated a strain similar to *Mycobacterium tuberculosis*. It was thought to be infectious only in 1720, when the treatment for tuberculosis became sanatorium care. It was only in the 19th century that Robert Koch famously isolated the tubercle bacilli and established an association between this bacillus and the tuberculosis disease [4].

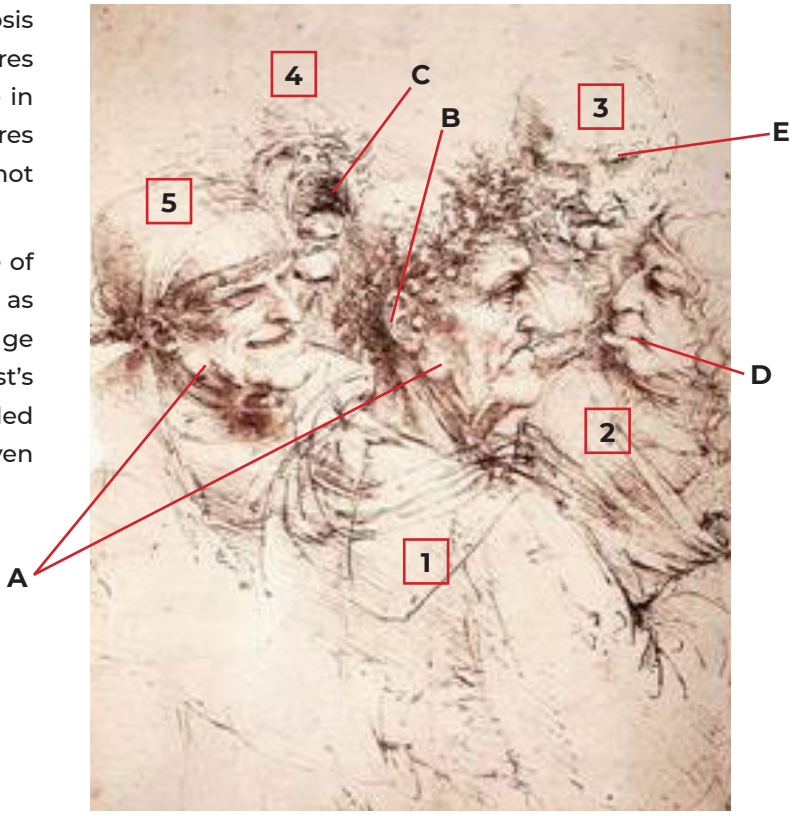
In the sketch, "The Five Grotesque heads", there are several clinical features of facial tuberculosis noted. The men, labelled as 1 and 5, have a swelling at the angle of the mandible (marked by red arrows as A) suggestive of tuberculosis of the jaw causing abscess, known as a lumpy jaw [5]. The man labelled 1 also shows a nodule over his ear(marked with a red arrow as B) which could be a papulo-nodular lesion of Lupus vulgaris [6].

The ugly old man, labelled as 2, is shown to have a prominent lower lip which is also called macrocheilia (marked with red arrow as D), which is also a manifestation of orofacial tuberculosis. The man, labelled as 3, has a prominent supra-orbital ridge over both eyes. The man, labelled as 4, is shown to have an open mouth with a mottled appearance of the pharynx. This is possibly a representation of oropharyngeal granulomas. The wide open mouth is likely to be secondary to a muscle spasm caused by tuberculosis of the temporo-mandibular joint. The last man, labelled as 5, shows poor dentition with loss of teeth, which is a common feature in tuberculous gingivitis which causes loss of alveolar bone and subsequent loss of teeth [7].

A plausible differential diagnosis to the features depicted in this sketch could include leprosy. It is not possible to differentiate between these two infectious conditions from the details shown in

the sketch. However, the diagnosis of sarcoidosis is unlikely, despite similar granulomatous features as its prevalence was less during Da Vinci's time in the Italian provinces and several distinct features of sarcoidosis such as Bell's palsy and uveitis is not detailed in the sketch [3].

This sketch gives us a glimpse of the importance of clinical signs found in infectious diseases such as tuberculosis and leprosy in a time where knowledge of these conditions was sparse. It also gives an artist's perspective of a pathology which has travelled through history and is of clinical significance even today.



Picture 1: 'The Five Grotesque Heads' by Da Vinci.

A-Swelling due to abscess in tuberculosis of jaw.
B- Nodular lesion of Lupus vulgaris.
C-Oropharyngeal granulomas inn a wide open mouth.
D- Prominent lower lip or macrocheilia.
E- Prominent supra-orbital ridge.

References

[1] Tillmann B. 1995. Die anatomischen Zeichnungen des Leonardo da Vinci [Anatomic drawings by Leonardo da Vinci]. Fortschr Kiefer Gesichtschir 40:5-11. German. PMID: 7557784.

[2] Trutty-Coohill P. 1998. Bracketing Theory in Leonardo's Five Grotesque Heads. In: Tymieniecka AT. (eds) Enjoyment. Analecta Husserliana (The Yearbook of Phenomenological Research), vol. 56. Springer, Dordrecht.

[3] Tan M, Harling L, Ashrafian H. 2014. Leonardo da Vinci's Five Grotesque Heads: early evidence of cranio-facial mycobacterial infection. Infection 42(4):795-796.

[4] Barberis I, Bragazzi NL, Galluzzo L, Martini M. 2017. The history of tuberculosis: from the first historical records to the isolation of Koch's bacillus. Journal of Preventive Medicine and Hygiene. 58(1):E9.

[5] Gupta KB, Manchanda M, Yadav SP, Mittal A. 2005. Tubercular osteomyelitis of mandible. Indian J Tuberc. 52:147–50.

[6] Rullán J, Seijo-Montes RE, Vaillant A, Sánchez NP. 2012. Cutaneous Manifestations of Pulmonary Disease. In: Sánchez NP, editor. Atlas of Dermatology in Internal Medicine. New York: Springer Science and Business Media; 2012. [Last accessed on 2015 Jun 22]. pp. 17–30. Available from: http://www.springer.com/978-1-4614-0687-7

[7] Bansal R, Jain A, Mittal S. 2015. Orofacial tuberculosis: Clinical manifestations, diagnosis and management. J Family Med Prim Care 4(3):335-341. doi:10.4103/2249-4863.161312

3 CASE REPORTS

Disseminated cryptococcosis in an immunocompetent child

Nitin Gupta[1,2], Suhas Reddysetti[3], Vishwapriya Mahadev Godkhindi[4], Shreeya Aswath[5], Archana Mevalegire Venkatagiri[6], Vasudeva Bhat K[6], Kalasekhar Vijayasekharan[6], Kavitha Saravu[1,2]

[1] Department of Infectious Diseases, Kasturba Medical College, Manipal Academy of Higher Education, Manipal, Karnataka, India, 576104

[2] Manipal Center for Infectious Diseases, Prasanna School of Public Health, Manipal Academy of Higher Education, Manipal, Karnataka, India, 576104

[3] Department of Medicine, Kasturba Medical College, Manipal Academy of Higher Education, Manipal, Karnataka, India, 576104

[4] Department of Pathology, Kasturba Medical College, Manipal Academy of Higher Education, Manipal, Karnataka, India, 576104

[5] Department of Paediatrics, Kasturba Medical College, Manipal Academy of Higher Education, Manipal, Karnataka, India, 576104

[6] Division of Paediatric Haemato-oncology, Department of Paediatrics, Kasturba Medical College, Manipal Academy of Higher Education, Manipal, Karnataka, India, 576104

ABSTRACT

Disseminated cryptococcosis primarily affects the immunocompromised individuals with central nervous system as the most common site of dissemination. We report a rare case of disseminated cryptococcosis in a 11-year old girl who presented with pulmonary involvement, hepatosplenomegaly and generalized lymphadenopathy. She responded completely to anti-fungal therapy (flucytosine and amphotericin followed by fluconazole).

Keywords

Cryptococcus spp; Pulmonary; lymphadenopathy

Introduction

Cryptococcosis is an invasive fungal infection reported from around the world [1]. It is caused by *Cryptococcus neoformans* or *gattii* [2]. Although it primarily affects immunocompromised individuals, it is increasingly being reported from immunocompetent hosts as well. The common risk factors for cryptococcus infection include human immunodeficiency virus (HIV) infection, immunosuppressive therapy, transplantation, malignancies and idiopathic CD4 lymphopenia [2]. Pulmonary cryptococcosis is often self-limiting and may go undiagnosed [3]. In individuals with a history of immunosuppression, the fungus may disseminate to other organs, including the central nervous system. Reports of disseminated cryptococcosis in apparently immunocompetent individuals are relatively rare. We report one such case of disseminated cryptococcosis in an apparently immunocompetent child.

Case report

An 11-year-old girl presented with intermittent high-grade fever and dull aching diffuse abdominal pain for one and half month. Ten days prior to the presentation, she developed progressive respiratory distress and yellowish discolouration of eyes. At presentation, she was hypoxic and required non-invasive ventilation to maintain saturation. On examination, she was found to have generalized lymphadenopathy involving bilateral cervical (Levels Ib, II, III and IV) and axillary lymph nodes (anterior and central). She was also found to have hepatosplenomegaly. She had no signs of meningeal irritation.

Her routine laboratory and biochemical parameters showed leukocytosis (24,000/cu.mm), increased bilirubin (Total-6.4 mg/dl, Direct-5.7 mg/dl), alkaline phosphatase (882 U/l) and elevated transaminases (Aspartate transaminase-115 IU/L, Alanine transaminase-49 IU/L). Contrast-enhanced computed tomography (CECT) of the chest showed the presence of bilateral interstitial thickening, bilateral consolidation in lower lobes, centrilobular nodules and mediastinal lymphadenopathy. CECT of the abdomen showed hepatosplenomegaly (liver-17 cm, spleen-11 cm), retroperitoneal lymph nodes (coeliac trunk, porta hepatis, pre- and para-aortic). The left axillary lymph node was biopsied, which showed non-caseating granulomas and presence of yeast like forms of *Cryptococcus* spp. (Figure 1). This was confirmed by mucicarmine staining. A serum cryptococcal antigen was done, which was also positive. Lumbar puncture was deferred due to the absence of headache and neck signs. She was found to be negative for HIV-1 and 2 by serology. Her immunoglobin levels (G, A, M) were normal. Her evaluation for chronic granulomatous disease by Nitroblue Tetrazolium test was negative. Subset analysis of lymphocytes on flow cytometry showed the following results: CD45+ cells- 4900/mcl, CD3+T cells-4081/mcl, CD4+ cells- 1919/mcl, CD8+ cells-2044/mcl, CD4/CD8 ratio-0.93, CD19+B cells-506/mcl (10.3%), CD56+NK cells- 294/mcl (6%).

She was treated with liposomal amphotericin B (3 mg/kg) and flucytosine (100 mg/kg/day) for two weeks. Her fever and respiratory distress improved in five days. Her lymph nodes reduced significantly, and liver functions improved with the induction therapy. She was discharged after two weeks of admission on eight weeks of consolidation therapy with fluconazole (12 mg/kg). Her lymph nodes had completely regressed after the completion of consolidation therapy, and she was planned for one year of maintenance therapy with fluconazole (6 mg/kg).

Discussion

The mode of acquisition of cryptococcosis is by inhalation of the spores that get deposited in the smaller airways [4]. Most of the individuals with this early infection remain asymptomatic, but a small fraction of these patients may develop the symptomatic pulmonary disease [3]. Eventually, the fungus may disseminate from lungs to other sites of the body like the brain, peripheral lymph nodes and skin. The determinants for the development of symptomatic or disseminated disease are the immune status of the host and the burden of inhaled spores. This is the reason why disseminated cryptococcosis is more common in patients with an impaired immune function such as HIV. In HIV-uninfected patients, other underlying condition that has been identified includes liver cirrhosis, diabetes mellitus and autoimmune diseases [5,6]. However, no immunosuppressive condition was identified in our patient.

The gold standard for diagnosis of cryptococcosis is antigen detection test, either from the tissue/fluid or serum [7]. However, isolation of *Cryptococcus* spp. from a clinical specimen, or demonstration of typical capsular yeast forms on histological staining of tissues is equally helpful [7]. In our patient, cryptococcosis was not kept as a differential in the beginning, and therefore, only the histopathological specimens were sent, which demonstrated the typical budding capsulated yeast forms. Lumbar puncture was not done in our patient as she was immunocompetent without any neurological symptoms or signs suggestive of involvement [8]. Although mild to moderate cases of pulmonary cryptococcosis can be managed with oral azoles, induction therapy with amphotericin and flucytosine is required in cases with severe/disseminated disease [8]. Considering the severe pulmonary involvement and features suggestive of dissemination (hepatosplenomegaly, generalized lymphadenopathy), she was managed with intravenous amphotericin and flucytosine in the first two weeks followed by fluconazole.

We report this case to highlight the possibility of cryptococcosis in immunocompetent patients with pulmonary involvement, generalized lymphadenopathy and hepatosplenomegaly without any significant history of exposure in endemic areas.

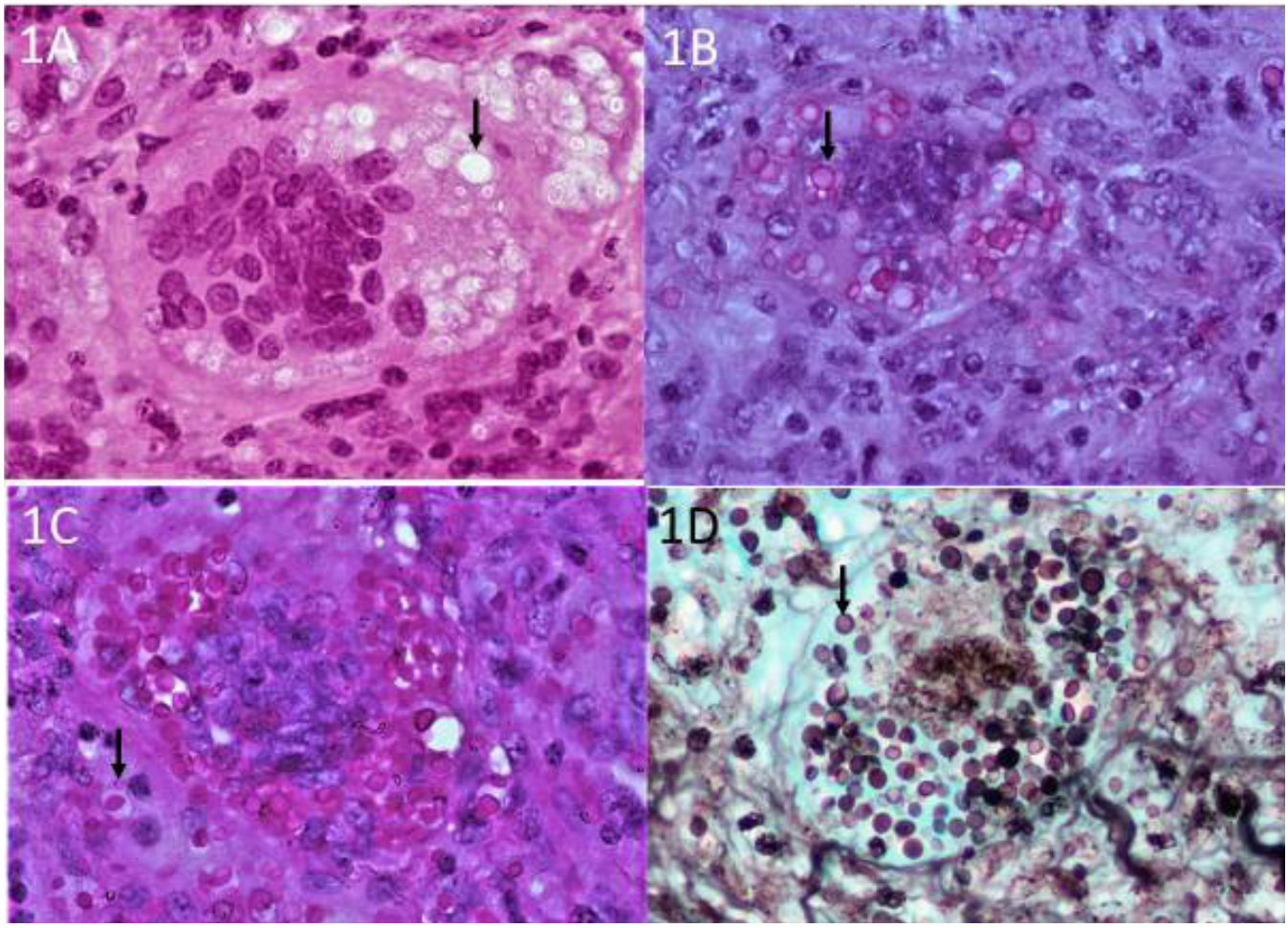


Figure 1: Haematoxylin and eosin stain (600x) showing multiple intracellular and extracellular capsulated yeast forms with foreign body type giant cell (1A). Mucicarmine (600x) stain showing the gelatinous mucopolysaccharide capsule (1B). Periodic acid Schiff (600x) stain showing the magenta-pink stained thick-walled yeast forms (1C). Gomori's methenamine silver (600X) stain showing the black stained yeast forms (1D).

References

[1] Herkert PF, Hagen F, Pinheiro RL, Muro MD, Meis JF, Queiroz-Telles F. 2017. Ecoepidemiology of Cryptococcus gattii in Developing Countries. J Fungi Basel Switz. 3:3(4).

[2] Kwon-Chung KJ, Fraser JA, Doering TL, Wang Z, Janbon G, Idnurm A, et al. 2014. Cryptococcus neoformans and Cryptococcus gattii, the etiologic agents of cryptococcosis. Cold Spring Harb Perspect Med. 4(7):a019760.

[3] Wu H-H, Chen Y-X, Fang S-Y. 2020. Clinicopathological features of isolated pulmonary cryptococcosis in HIV-negative patients. J Int Med Res. 48(6):300060520927877.

[4] Velagapudi R, Hsueh Y-P, Geunes-Boyer S, Wright JR, Heitman J. 2009. Spores as infectious propagules of Cryptococcus neoformans. Infect Immun. 77(10):4345–55.

[5] Chuang Y-M, Ho Y-C, Chang H-T, Yu C-J, Yang P-C, Hsueh P-R. 2008. Disseminated cryptococcosis in HIV-uninfected patients. Eur J Clin Microbiol Infect Dis. 27(4):307–10.

[6] Hou X, Kou L, Han X, Zhu R, Song L, Liu T. 2019. Pulmonary cryptococcosis characteristics in immunocompetent patients-A 20-year clinical retrospective analysis in China. Mycoses. 62(10):937–44.

[7] Skipper C, Abassi M, Boulware DR. 2019. Diagnosis and Management of Central Nervous System Cryptococcal Infections in HIV-Infected Adults. J Fungi Basel Switz. 5(3).

[8] Baddley JW, Perfect JR, Oster RA, Larsen RA, Pankey GA, Henderson H, et al. 2008. Pulmonary cryptococcosis in patients without HIV infection: factors associated with disseminated disease. Eur J Clin Microbiol Infect Dis. 27(10):937–43.

EBV positive diffuse large B-cell lymphoma-NOS: A case report

Prashanth B[1], Pooja K Suresh[2], Nirupama M[2]

[1]Department of Medicine

[2]Department of Pathology, Kasturba Medical College, Mangalore, Manipal Academy of Higher Education, Manipal.

Case Report

A 57-year-old male presented to the hospital with a complaint of fever since 6 months. Fever was insidious in onset, intermittent in nature. The fever episodes were once or twice weekly initially, later progressed to three-four times per day. The fever was associated with chills and rigors, nausea, right hypochondriac pain in the abdomen and weight loss of 15 kgs in the past 3 months which did not show any aggravating or relieving factors. He also had decreased appetite since few months. Patient did not have any history of cough, breathlessness, fatigue, weakness or body pains. The patient did not have any associated co-morbidities, but was put on treatment with empirical antibiotics for typhoid. History of hospitalisation for the same where the patient was given multiple IV antibiotics (Amikacin, cefoperazone sulbactum and doxycycline) 1 month back but the fever did not subside. The patient consumes a mixed diet and used to consume alcohol and was a smoker but stopped 30 years back. Bowel and bladder habits were regular.

On examination, his pulse was 90 beats per minute, blood pressure was 110/70 mm of Hg, respiratory rate of 18 cycles per min and jugular venous pressure 8 cm of H_2O. Per abdomen examination revealed tender hepatomegaly and splenomegaly 4 cm below the costal margin. Rest of the abdomen was soft and bowel sounds were heard.

Laboratory investigation revealed a haemoglobin of 8.3 gm/dL, total leucocyte counts of 5900 and platelet count of 1,62,000/mm3. Erythrocyte sedimentation rate was 84 mm/hour. The differential counts showed neutrophils 77%, lymphocytes 7% and monocytes 16%. Peripheral smear revealed microcytic hypochromic anemia with lymphopenia. Bone marrow aspirate showed hypercellular marrow with granulocytic hyperplasia and macrophage activity. Bone marrow biopsy also showed nonspecific granulocytic hyperplasia. There was absence of abnormal cells in the peripheral blood and bone marrow examination.

Biochemical investigations revealed urea 25 mg/dL, creatinine 0.61 mg/dL, sodium 137 mg/dL, potassium 4.02 mmol/L, chloride 107.5 mmol/L, bicarbonate 18.4 mmol/L, uric acid 2.8 mg/dL and random blood sugar 110 mg/dL. Liver function test showed total bilirubin 1.51 mg/dL, direct bilirubin 0.65 mg/dL, total proteins 5.6 g/dL, albumin 3.1 mg/dL, AST 23U/l, ALT 31 U/l, ALP 86 IU/l, INR 1.16, APTT 52.3 sec, Thyroid stimulating hormone 2.48 mIU/L, C-reactive protein 197 mg/L (Positive), Lactate dehydrogenase 354 U/L, ferritin 2456 mg/L and triglycerides 318 mg/dL.

Malraia, brucella antigen and Weil Felix testswere negative. Blood culture and urine culture was negative. Antinuclear antibodies (ANA) and stool occult blood was negative. Preliminary blood investigations showed features of secondary hemophagocytic lymphohistiocytosis (HLH) features. Hence patient was further worked up for cytomegalovirus (CMV), Epstein Barr virus (EBV) infections as a part of pyrexia of unknown origin work up. Chest radiography (Figure 1) showed hyperinflated bilateral lung fields with flattened bilateral hemidiaphragm suggestive of emphysema.

Electrocardiogram was normal, with absence of any vegetations. Computed tomography (CT) of chest and abdomen was done which showed hepatomegaly and borderline splenomegaly with multiple retroperitoneal lymph nodes. There was absence of mediastinal lymphadenopathy. CT

guided fine needle aspiration and Tru-Cut biopsy of the lymph node was planned.

Fine needle aspiration (Figure 2AB) of retroperitoneal lymph node revealed cellular smears composed of polymorphic population of abnormal lymphoid cells composed of large and intermediate cells having scant cytoplasm, large nucleus with coarsely clumped chromatin with few showing distinct nucleolus admixed with reactive small lymphocytes and histiocytes.

Tru-Cut biopsy of the retroperitoneal lymph node was done which showed complete effacement of normal lymph node architecture with diffuse infiltration by abnormal lymphoid cells composed of large and intermediate cells and focal areas of necrosis. The background showed a reactive population of small lymphocytes and histiocytes (Figure 3AB). Immunohistochemistry was performed which showed neoplastic cells positive for CD20 (Figure 3C), Bcl6 (Figure 3E), MUM1 (Figure 3F) and negative for CD3 (Figure 3D), CD5, Bcl2 on the abnormal lymphoid cells. The MIB index was 92% (Figure 3G). Features were of Non germinal center type diffuse large B cell lymphoma.

Meanwhile serum EBV quantitative viral load done by real time PCR was positive with 426,515 copies/ml. Since the facility for in-situ hybridization for EBER was not available, we did IHC EBV antibody-LMP1 on the biopsy which showed nuclear positive in the abnormal lymphoid cells (Figure 3H). The final diagnosis was rendered as EBV positive diffuse large B cell lymphoma- Not otherwise specified (EBV positive DLBCL-NOS).

Patient is presently on treatment for DLBCL with R-CHOP chemotherapy with resolution of secondary HLH features with normalization of ferrittin levels. He is currently afebrile with increased appetite. So far he has completed 2 cycles of chemotherapy. A total of 6 cycles of chemotherapy are planned with an interim PET-CT and interim EBV titres post 3 cycles of chemotherapy.

EBV-positive diffuse large B-cell lymphoma, NOS, is an entity included in the 2016 WHO classification of lymphoid neoplasms, which is an EBV-positive clonal lymphoid proliferation. It accounts for <5 – 15 % of DLBCLs. It is usually seen in patients in 8th decade with a male preponderance (M:F = 1.2-3.6 : 1). EBV positive DLBCL is believed to be associated with immunosenescence in older patients. They are known to involve nodal and extranodal sites such as lungs and GIT. Clinical features at presentation are variable. More than half of the cases show high / high-intermediate International Prognostic Index (IPI) score. In-situ hybridization for EBV-encoded small RNA (EBER) is mandatory for the diagnosis of EBV positive DLBCL. With age cut-off point of 45 years, the prognosis of EBV-positive DLBCL differs significantly between elderly and young patients. It is an aggressive lymphoma with median survival of about 2 years in elderly, even when treated with rituximab immunochemotherapy. While in younger patients, these cases are known to have an excellent prognosis, with long-term remission in > 80 % of the cases [1,2].

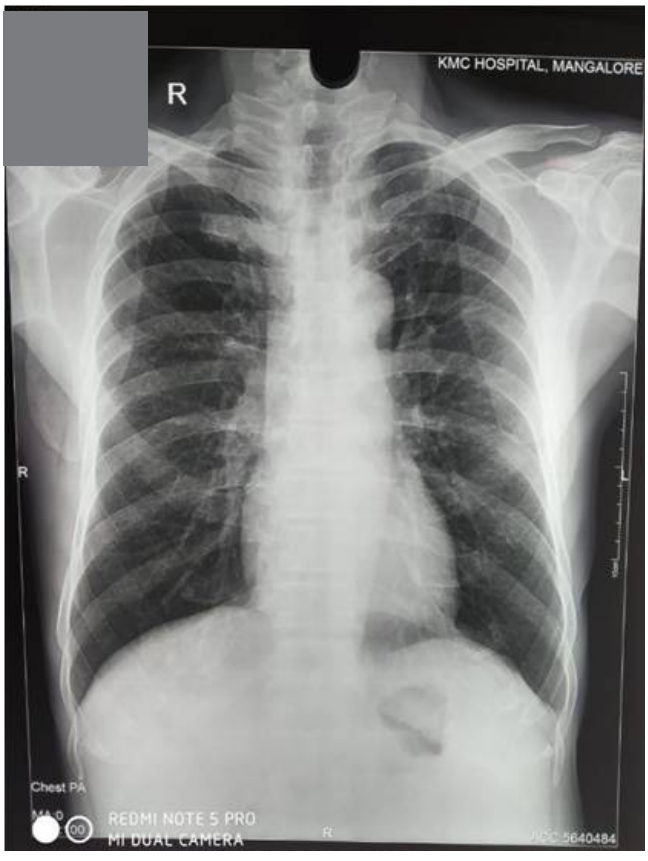


Figure 1: Chest X ray showed hyper inflated bilateral lung fields with flattened bilateral hemi diaphragm suggestive of emphysema.

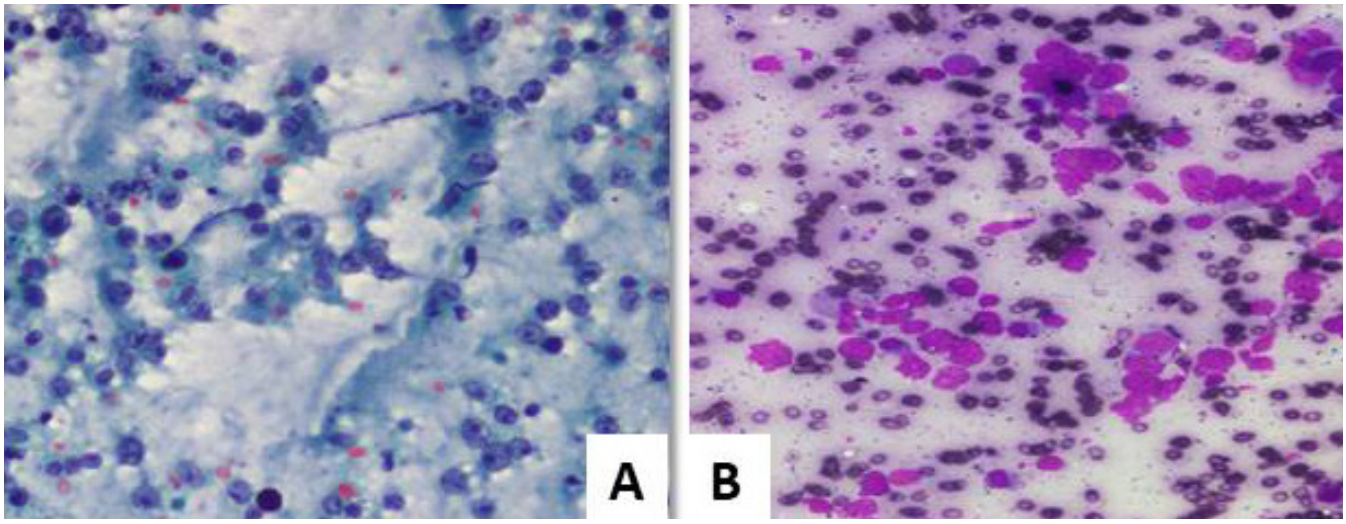


Figure 2AB: Cytology of retropeitoneal lymph node revealed cellular smears composed of polymorphic population of abnormal lymphoid cells composed of large and intermediate cells having scant cytoplasm, large nucleus with coarsely clumped chromatin with few showing distinct nucleolus admixed with reactive small lymphocytes and histiocytes (400x, PAP stain; 400x, MGG stain).

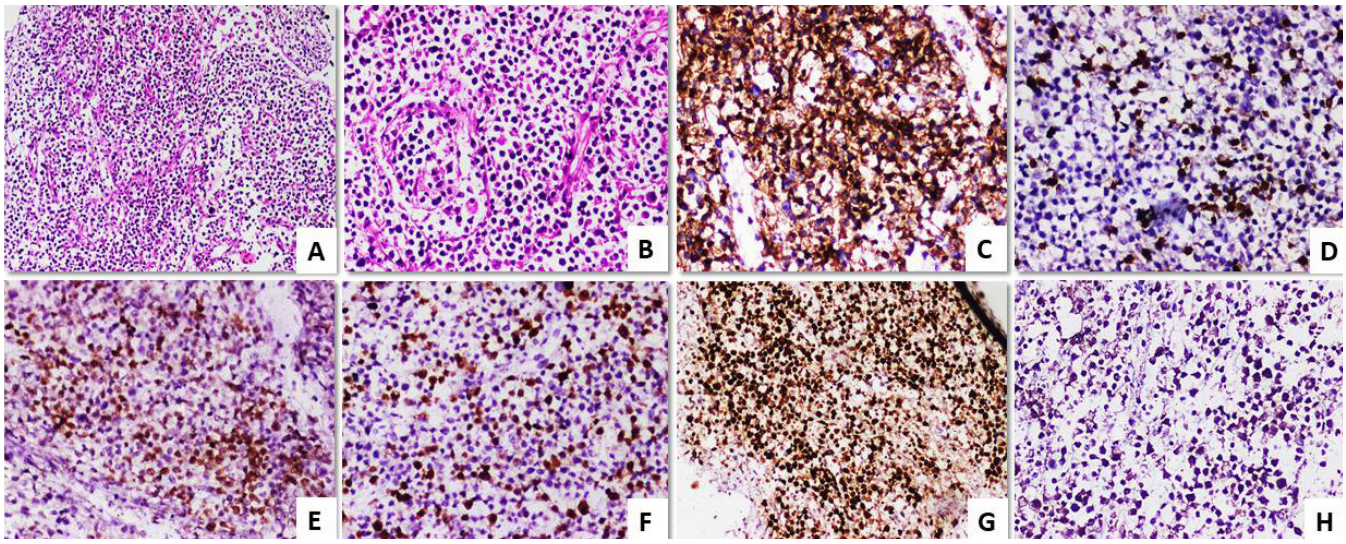


Figure 3: Histomorphology and immunohistochemistry of retropeitoneal lymph node: AB: Histology showed complete effacement of normal lymph node architecture with diffuse infiltration by abnormal lymphoid cells composed of large and intermediate cells. (40x, HE stain; 100x, HE stain). C: CD20 IHC positive in neoplastic cells (100x, CD20 antibody); D: CD3 IHC negative in neoplastic cells, positive in reactive lymphoid cells (40x, CD3 antibody); E: Bcl6 IHC positive in neoplastic cells (40x, Bcl antibody); F: MUM1 IHC positive in neoplastic cells (40x, MUM antibody); G: KI67 IHC MIB index:92% (40x, Ki67 antibody); H: EBV IHC positive in neoplastic cells (40x, EBV antibody).

References

[1] Castillo JJ, Beltran BE, Miranda RN, Young KH, Chavez JC, Sotomayor EM. 2018.EBV-positive diffuse large B-cell lymphoma, not otherwise specified: 2018 update on diagnosis, risk-stratification and management. Am J Hematol. 93(7):953-962. doi: 10.1002/ajh.25112. PMID: 29984868.

[2] Murthy SL, Hitchcock MA, Endicott-Yazdani TR, Watson JT, Krause JR. 2017. Epstein-Barr virus-positive diffuse large B-cell lymphoma.Proc (Bayl Univ Med Cent). 30(4):443-444. doi:10.1080/08998280.2017.11930222

Cryptic Clues from an Acute Abdomen - A Case of Disseminated Cryptococcosis

Archith Boloor[1], Ashwini M V[2], Vivek Koushik[3]

[1,2]Department of Internal Medicine, Kasturba Medical College, Manipal Academy of Higher Education, Mangalore

[3]Department of Nephrology, Apollo Hospitals, Chennai

Introduction

Cryptococcosis is one of the AIDS defining infections, seen particularly with advanced disease. The commonly affected sites are respiratory system and central nervous system. Disseminated cryptococcosis, particularly with peritonitis is an uncommon manifestation of cryptococcal infection. Here we discuss a case of 28 year old female, incidentally detected to be RVD positive, presenting with cryptococcal appendicitis with pelvic abscess and on further evaluation found to have disseminated cryptococcosis in the form of meningitis, mesenteric lymphadenitis and cryptococcuria.

Case report

28 year old female, homemaker, hailing from Chikkamagaluru, presented to the casualty of District Wenlock Hospital, Mangalore with complaints of right lower abdominal pain since 7 days and multiple episodes of non-projectile, non-bilious vomiting on the day prior to admission. History of low grade intermittent fever with headache was present since 20 days. Headache was bifrontal in localization, throbbing type. No history of loose stools/ jaundice/ abdominal distension/ mass per abdomen. No previous known comorbidities.

On examination, right ileac fossa tenderness was present with rebound tenderness and guarding. USG abdomen done showed free fluid in the pelvis and right ileac fossa probe tenderness was present, features suggestive of appendicitis with appendicular perforation. Serology was found to be positive for RVD on pre-operative workup. Open appendicectomy with drainage of pelvic abscess was done. Pus was sent for C/S and omental biopsy and appendix specimen was sent for HPE. On HPE, there was transmural granulomatous inflammation and fungal spores were seen (Figure 1). For confirmation, special stains GMS and PAS was done, which were positive suggesting the diagnosis of cryptococcal appendicitis (Figure 2,3). Diagnosis of Histoplasmosis was excluded as mucicarmine stain was negative. Urine routine showed 2 to 3 pus cells and yeast like budding cells. PAS stain done in urine sample was also positive (Figure 4).

On post operative day 3, patient complained of worsening headache. On examination,neck stiffness was present. No focal neurological deficits. Fundus examination was normal. CT brain done was normal. LP and CSF analysis done revealed a total cell count of 50, all lymphocytes. CSF CBNAAT was negative for TB. However, India Ink staining was positive and Cryptococcus neoformans was grown after 48 hours of incubation. CD4 count done was 98. Patient was started on injection amphotericin B and tablet fluconazole. Injection mannitol and dexamethasone was also added. Cotrimoxazole double strength tablet once daily was started for PCP prophylaxis.

Repeat LP done after 14 days of amphotericin B showed persistent India Ink positivity. Hence, fluconazole was continued for 8 weeks. MRI Brain with contrast showed cryptococcomas. CECT abdomen done in view of persistent drain output on post operative day 9 showed multiple enlarged mesenteric lymph nodes.

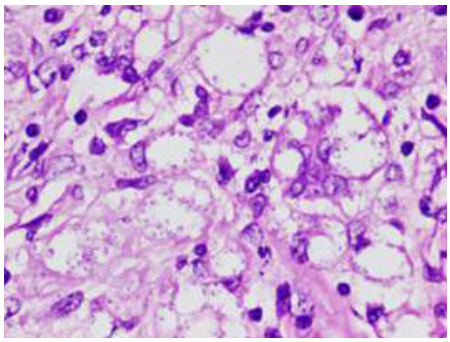


Figure 1:
Presence of fungal spores on H and E

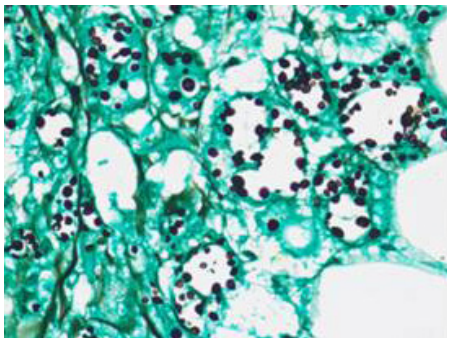


Figure 3:
Special stain-PAS Positivity

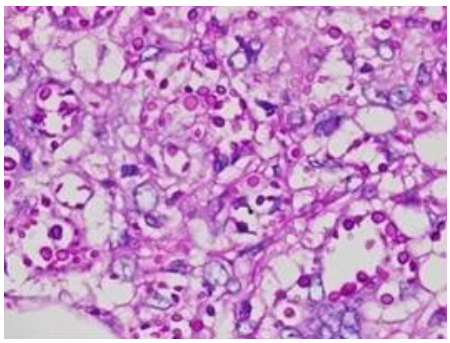


Figure 2:
Special stain-GMS Positivity

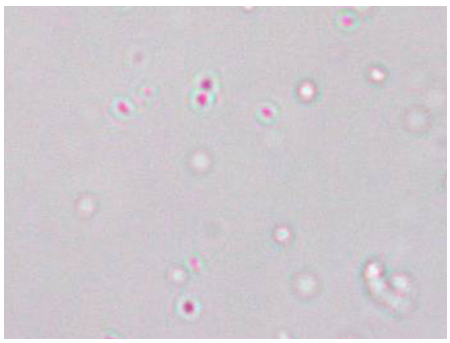


Figure 3:
PAS stain positive in urine sample

Discussion

Cryptococcosis is an invasive fungal infection, more prevalent in immunocompromised. Most cases are observed with CD4 count of <100 cells/microL. Although the use of HAART has significantly lowered the incidence of cryptococcosis, the estimated global burden of HIV associated cryptococcal meningitis approximates 1 million cases annually worldwide [1].

Most common presentations of cryptococcosis are pulmonary infection and meningitis. Cryptococcal peritonitis is a rare manifestation and among these patients, the incidence of positive samples of CSF and urine were 16.4% and 8.2% respectively [2]. Although diagnosis of cryptococcal peritonitis requires a high index of suspicion, it should be in the list of differential diagnosis when evaluating a patient with peritonitis especially with concomitant immunocompromised state.

Treatment consists of a primary induction therapy with Amphotericin B(0.7–1.0 mg/kg per day IV) plus flucytosine (100 mg/kg per day orally in 4 divided doses; IV formulations may be used in severe cases) for at least 2 weeks. Consolidation therapy consists of fluconazole (400 mg [6 mg/kg] per day orally) for a minimum of 8 weeks. This is followed by a maintenance suppressive therapy with oral fluconazole 200mg daily till CD4 cell count >100 cells/μL and an undetectable or very low HIV RNA level sustained for ≥3 months (minimum of 12 months of antifungal therapy) [3].

If the CSF culture after 2 weeks of treatment is reported to be positive after discontinuation of the induction regimen, reinstitution of atleast another 2 week induction course should be considered.

Concluding, disseminated cryptococcosis is a rare entity and requires early initiation and prolonged antifungal therapy.

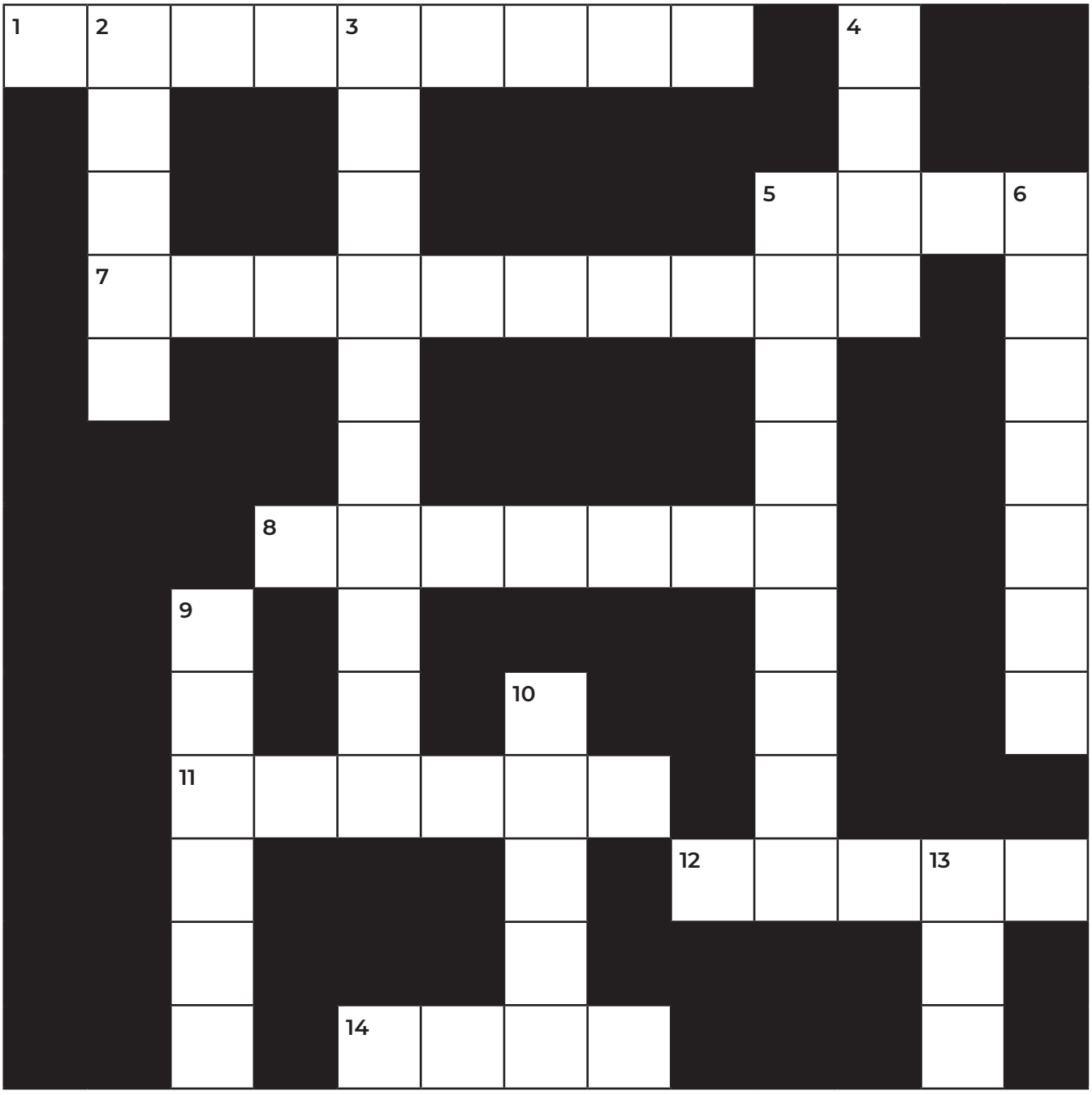
References

[1] Park BJ, Wannemuehler KA, Marston BJ, et al. 2009. Estimation of the current global burden of cryptococcal meningitis among persons living with HIV/AIDS. AIDS 23:525-530

[2] El-Kersh K, Rawasia WF, Chaddha U, Guardiola J. 2013. Rarity revisited: cryptococcal peritonitis. Case Reports. 2013:bcr2013009099

[3] Perfect JR, Dismukes WE, Dromer F, Goldman DL, Graybill JR, Hamill RJ, et al. 2010. Clinical Practice Guidelines for the Management of Cryptococcal Disease: 2010 Update by the Infectious Diseases Society of America. Clin Infect Dis. 50:291-322.

4 Crossword - To Keep the Grey Matter Ticking



Across

1. Inflammation of airsacs
5. Retrovirus causing lymphoma in humans
7. One of the symptoms associated with dog bite
8. Endemic protozoal infection in India
11. Disease transmitted through *Xenopsylla cheopis*
12. Intra cytoplasmic viral inclusion bodies
14. Bacteria associated with serious skin and soft tissue infections

Down

2. A zoonotic disease outbreak through fruit bats
3. Cell wall deficient pleuro pneumonia like organism
4. The virus, Dr. Gagandeep Kang is associated with....
6. Agent that induces artificial active immunity
9. A syndrome due to bacterial endotoxins
10. Viral infection with orchitis as most common complication
13. An ectoparasite of this animal transmits Bubonic Plague

SECTION

4

Pictus...

MAC ID in Pictures...

3rd Manipal International Infectious Diseases Conference

10th and 11th August 2019

Guest lecture by Dr. Jesse Papenburg

12th August 2019




Guest lecture by Dr. Sheela Shenoi

29th October 2019



Symposium on HIV and Inauguration of Department of Infectious Diseases

4th November 2019

Symposium on HIV – KMC, Mangalore

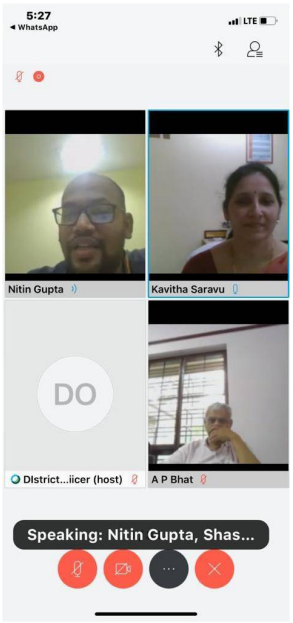
5th November 2019

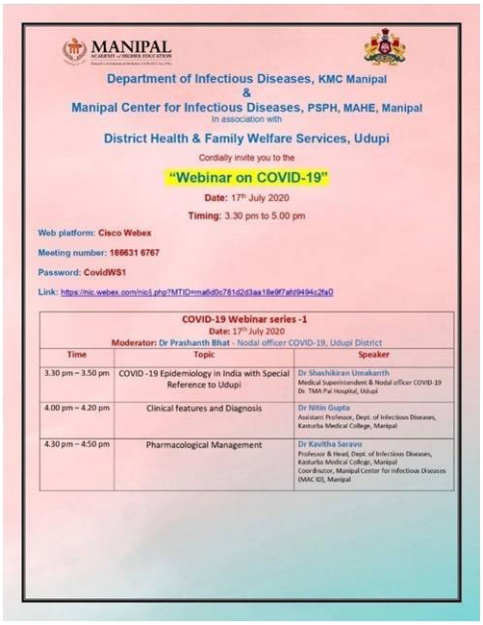
Symposium on Infectious Diseases outbreaks

25th January 2020

Webinar series on COVID-19

17th and 25th July, 2020



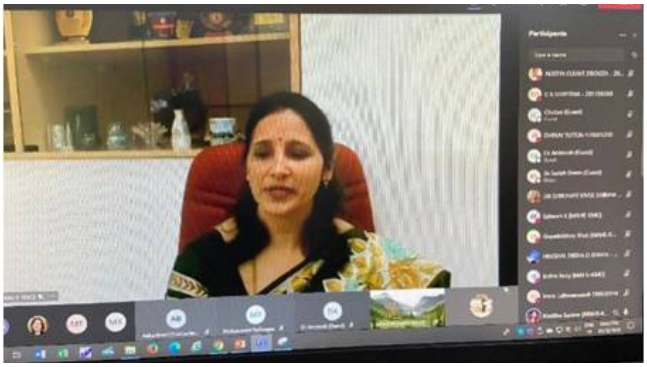


HIV Update 2020 – KMC, Mangalore

30th November 2020

Virtual World AIDS Day Symposium

1st December 2020



SECTION

5

Laurus...

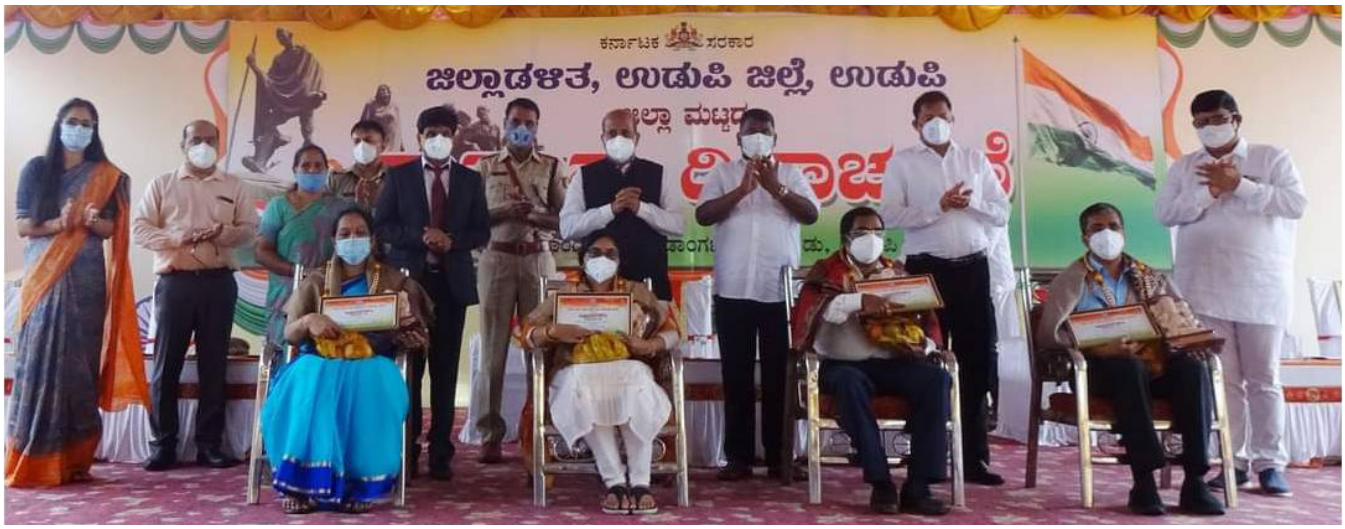
MAC ID Faculty achievements...

[A] Awards/ Recognition of MAC ID Members

(I) Recognitions

Award for COVID-19 warriors in Kasturba Hospital, Manipal, from MAHE on the eve of 74th Independence Day, 15th August 2020

Dr. Kavitha Saravu received an award from District Collector of Udupi – COVID-19 warrior



Dr. Shashikran Umakanth received an award from District Collector of Udupi – COVID-19 warrior

Dr. Neetha Shenoy, Senior lecturer, Department of Conservative Dentistry and Endodontics, MCODS, Manipal won the Best Essay Award in the Faculty category on the topic “Cariology in India-A chance or a challenge”. The essay competition was organized by Department of Cariology, Saveetha Dental College, Chennai.

Dr. Neetha Shenoy, also won the Second Prize in the National Level Essay Competition 2020 conducted by the Indian Society of Periodontology on the topic “Periodontal treatment protocol in general practice”.

(II) Projects

Sl. No	Name of the funding agency	Investigators	Project title	Amount Sanctioned
1	Charité – Berlin Institute of Health, Berlin, Germany	**Dr. Kavitha Saravu** Department of Infectious Diseases, KMC, Manipal	Point-of-care ultrasound to improve diagnosis and management of respiratory infectious diseases in Manipal, India	INR 5,46,176/-
2	ICMR	**Dr. Chythra R Rao** Dept. of Community Medicine, KMC, Manipal **CoI - Dr. Suma Nair,** Dept. of Community Medicine, KMC, Manipal **Dr. Chiranjay Mukhopadhyay,** Dept. of Microbiology, KMC, Manipal **Dr. Manthan Janodia** MCOPS, Manipal	Socio-cultural and environmental drivers of antibiotic resistance in the community: people, physicians and pharmacists' perspective – a mixed methods approach	INR 27,20,933/-
3	FIND andMcGill International TB Center, Canada	**Dr. Kavitha Saravu** Department of Infectious Diseases, KMC, Manipal, **Dr. Madhukar Pai** Director, McGill International TB center, Canada	Towards a rapid biomarker-based diagnostic test for active tuberculosis	INR 37,61,650/-
4	IC-IMPACTS (India-Canada Centre for Innovative Multidisciplinary Partnerships to Accelerate Community Transformation and Sustainability)	**Dr. Nitika Pant Pai** Associate Professor of Medicine, McGill University Divisions of Clinical Epidemiology & Infectious Diseases, McGill University Health Centre, Canada **Dr. Suma Nair** Department of Community Medicine, KMC, Manipal	Smart app-based rapid multiplex screening of HIV associated co-infections of at risk populations at the point-of-care: A demonstration study in India	CAD $25,000/-
5	SERB	**Dr. Kavitha Saravu** Department of Infectious Diseases, KMC, Manipal **Dr. Chunduru Kiran** Department of Infectious Diseases, KMC, Manipal	Scrub typhus: Clinico-epidemiological analysis, humoral immune response and Molecular characterization of *Orientia tsutsugamushi*	INR 45,83,120/-

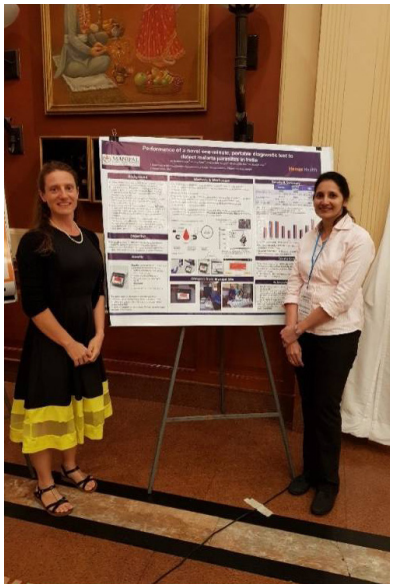
(III) Awards

I Prize for **Ms. Shilia Jacob Kurian** in Student's Pharmaceutical Conclave-2020

MAC ID Student Member

Ms. Shilia Jacob Kurian, Research Scholar, Dept. of Pharmacy Practice, MCOPS won the Second Prize under Clinical Research stream in "Student's Pharmaceutical Conclave" organized by Pharmacist Society of Kerala, in association with Kerala Private Pharmacists Association (KPPA) on 21st August 2020. She received the prize for the online presentation for the research paper entitled "Multicentric observational study on protective effect of metformin against tuberculosis in diabetic patients in south-Indian tertiary healthcare facilities" under the guidance of Dr. Sonal Sekhar M, Dr. Navya Vyas and Dr. Manu Mohan. The research was supported by MACID Seed Grant from Manipal Center for Infectious Diseases, PSPH, MAHE, Manipal. Ms. Shilia is pursuing Ph.D. under the guidance of Dr. Sonal Sekhar M, Dept. of Pharmacy Practice, MCOPS, Manipal.

(IV) International Conference presentations



Asia Pacific Malaria Elimination Network Meeting at Kathmandu, Nepal, October 15th-16th, 2019

Dr. Kavitha Saravu was invited as a member for Resistance Research group for virtual workshop on 'Addressing the threat of antimalarial drug resistance to malaria elimination in South East Asia', on 28th–29th October, 2020 organized by The Academy of Medical Sciences.

Dr. Nitin Gupta

Virtual Oral presentation, Research in Progress, Royal Society of Tropical Medicine and Hygiene (RSTMH), London, 2020. Clinical and laboratory profile of patients with Kyasanur forest disease: a single-centre study of 192 patients.

Virtual Poster Presentation, ECCVID 2020 (ESCMID Conference on Corona Virus Disease), Comparison of guidelines for COVID-19 therapeutics in India. 23rd -25th September 2020.

[B] Publications

(I) MAC ID Affiliated Articles

1. Gupta, N., John, A., Kokkottil, M.S., Varma, M.,Umakanth, S. and Saravu, K., 2021. Clinical profile and outcomes of asymptomatic vs. symptomatic travellers diagnosed with COVID-19: An observational study from a coastal town in South India. Drug Discoveries & Therapeutics. IF: 0.881, Q2
2. Pericherla, S., Gupta, N. and Saravu, C., 2021. Clinical profile and treatment outcomes of patients with brucellosis: a hospital-based cohort study from Southern India.Le Infezioni in Medicina, 1: 65-69. IF: 1.145, Q3
3. Shanbhag, V., Chaudhuri, S., Arjun, N.R., Gupta, N., Umakanth, S. and Saravu, K., 2021. Utility of awake prone positioning with low dose systemic corticosteroids in coronavirus disease 2019 acute respiratory distress syndrome patients: A case series. Indian J Respir Care 10:100-106.
4. Gupta, N., Chunduru, K., Safeer, M.K. and Saravu, K., 2021. Clinical and laboratory profile of patients with Kyasanur Forest Disease: A Single-centre study of 192 patients from Karnataka, India. Journal of Clinical Virology. IF:2.866, Q1
5. Sukumar, C.A., Tomar, S., Rai, S. and Saravu, K., 2020. Pseudohypoparathyroidism: A diagnosis that traverses specialities. Online Journal of Health Allied Sciences 19(3):12. IF: 0.184, Q4
6. Gupta, N., Saravu, K., Varma, M., Afsal, P.M., Shetty, S. and Umakanth, S., 2020. Transmission of SARS-CoV-2 infection by children: A study of contacts of index paediatric cases in India. Journal of Tropical Pediatrics. fmaa081. IF:0.940, Q2
7. Gupta, N., Varma, M. and Saravu, K., 2020. Difference in clinical presentation between the first and second phases of Kyasanur Forest disease: an experience from a teaching hospital in South India. Le Infezioni in Medicina 28(4):597-602.
8. Gupta, N., Wilson, W., Neumayr, A. and Saravu K., 2020. Kyasanur Forest disease: State-of-the-art review. QJM: An International Journal of Medicine. 16:hcaa310. IF: 2.529, Q3
9. Mallya, S.D., Reddy S.K.T., Kamath, A., Pandey, A. and Saravu, K., 2020. Determinants of metabolic syndrome and 5-year cardiovascular risk estimates among HIV-positive individuals from an Indian tertiary care hospital. AIDS Research and Treatment. IF: 0.882, Q2
10. Vyas, N., Kurian, S.J., Bagchi, D., Manu, M.K., Saravu, K., Unnikrishnan, M.K., Mukhopadhyay, C., Rao, M. and Miraj, S.S., 2020. Vitamin D in prevention and treatment of COVID-19: current perspective and future prospects. Journal of the American College of Nutrition1-14.IF: 2.43, Q2
11. Ali, N., Gupta, N. and Saravu, K., 2020. Malnutrition as an important risk factor for drug-induced liver injury in patients on anti-tubercular therapy: an experience from a tertiary care center in South India. Drug Discoveries & Therapeutics 14(3):135-138. doi:10.5582/ddt.2020.03029. IF: 0.881, Q2
12. Togun, T., Hoggart, C.J., Agbla, S.C., Gomez, M.P., Egere, U., Sillah, A.K., Saidy, B., Mendy, F., Pai, M. and Kampmann, B., 2020. A three-marker protein biosignature distinguishes tuberculosis from other respiratory diseases in Gambian children. EBioMedicine 58:102909.IF: 5.858, Q1
13. Prabhu, A., Nandagopal, G., Yegneswaran, P.P., Prabhu, V., Verma, U. and Mani, N.K., 2020. Thread integrated smart-phone imaging facilitates early turning point colorimetric assay for microbes. RSC Advances 10:26853-26861. DOI: 10.1039/d0ra05190j.IF: 3.1, Q1
14. Prabhu, A., Nandagopal, M.G., Yegneswaran, P.P., Singhal, H.R. and Mani, N.K., 2020. Inkjet printing of paraffin on paper allows low-cost point-of-care diagnostics for pathogenic fungi. Cellulose 27:7691-7701.IF: 4.2, Q1

15. Sulis, G., Adam, P., Nafade, V., Gore, G., Daniels, B., Daftary, A., Das, J., Gandra, S. and Pai, M., 2020. Antibiotic prescription practices in primary care in low-and middle-income countries: A systematic review and meta-analysis. PLoS Medicine 17:e1003139. IF: 11.675, Q1

16. Pai, M., 2020. Tuberculosis: the story after the Primer. Nature Reviews Disease Primers 6:29. IF: 32.274, Q1

17. Gupta, N., Varma, M., Sheshadri, S. and Saravu, K., 2020. Pulmonary nocardiosis in an elderly man. BMJ Case Reports 13:e234090.IF: 0.44,Q3

18. Nash, M., Kadavigere, R., Andrade, J., Sukumar, C.A., Chawla, K., Shenoy, V.P., Pande, T., Huddart, S., Pai, M. and Saravu, K., 2020. Deep learning, computer-aided radiography reading for tuberculosis: a diagnostic accuracy study from a tertiary hospital in India. Scientific Reports 10:210. IF: 4.011, Q1

19. Nafade, V., Huddart, S., Sulis, G., Daftary, A., Miraj, S.S., Saravu, K. and Pai, M., 2019. Over-the-counter antibiotic dispensing by pharmacies: A standardised patient study in Udupi district, India. BMJ Global Health 4:e001869. doi:10.1136/ bmjgh-2019-00186. IF:4.280, Q1

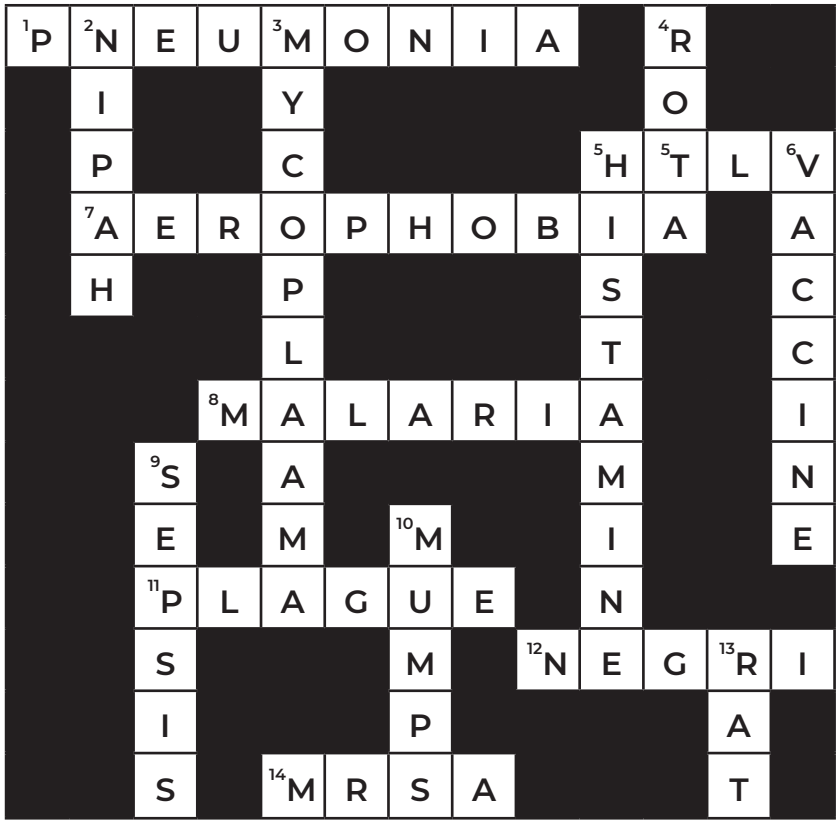
20. Prasada, S., Bhat, A., Bhat, S., Mulki, S.S. and Tulasidas, S., 2019. Changing antibiotic susceptibility pattern in uropathogenic *Escherichia coli* over a period of 5 years in a tertiary care center. Infection and Drug Resistance 12:1439-1443. doi: 10.2147/IDR.S201849.IF: 3.206, Q1

21. Talbot, E.A. and Pai, M., 2019. Tackling drug-resistant tuberculosis: we need a critical synergy of product and process innovations. The International Journal of Tuberculosis and Lung Disease 23(7):774–782. IF: 2.102, Q1

22. Saravu, K. and Pai, M., 2019. Drug-resistant tuberculosis: Progress towards shorter and safer regimens. Lung India 36:373-375. IF: 0.973, Q3

23. Mehta, C.H., Narayan, R., Aithal, G., Pandiyan, S., Bhat, P., Dengale, S., Shah, A., Nayak, U.Y. and Garg, S., 2019. Molecular simulation driven experiment for formulation of fixed dose combination of Darunavir and Ritonavir as anti-HIV nanosuspension. Journal of Molecular Liquids 293:111469. IF: 4.561, Q1

Crossword solutions (for Crossword on Pg. 45)



Contributed by:

Dr. Ashwini Hegde and **Dr. Pooja Rao**, Department of Microbiology, KMC, Mangalore

SECTION 6

Mustus...

Upcoming ID conference details...

National ID Conferences

International Conference on Latest Research on Corona Virus and its Vaccine (ICRCVV)
1st–2nd May, 2021
Ernakulam, Kerala, India
For more details, log on to: http://researchconferences.in/Conference/741/ICRCVV/

International Conference on Chronic Disorder & Infectious Diseases
14th–15th August, 2021
Live Stream
For more details, log on to: http://www.meetingfora.com/Conference/224/ICCDID/

International ID Conferences

Canadian Conference on HIV/AIDS Research 2021
5th–7th May, 2021
Virtual Conference, Canada
For more details, log on to: https://www.cahr-acrv.ca/conference/

Hepatitis C Virus and Related Viruses 27th International Symposium 2021
6th–9th July, 2021
Virtual Conference, Canada
For more details, log on to: https://www.hcv2021.org/home

World Congress on Infectious Diseases
9th–11th September, 2021
Rome, Italy
For more details, log on to: https://infectious-diseases-conferences.magnusgroup.org/

12th International Conference on Emerging Infectious Diseases
22nd – 23rd October, 2021
Rome, Italy
For more details, log on to: https://emerging-diseases.infectiousconferences.com/

18th Asia Pacific Congress of Clinical Microbiology and Infection
11th–13th November, 2021
Suntec, Singapore
For more details, log on to: https://www.apccmi2020.com/

The Immunotherapy for Infectious Diseases Conference - IIDC 2022
20th–23rd June, 2022
Pavia PV, ITALY
For more details log on to: https://www.idimmunotherapy.com/

Opportunities for MAC ID faculty members

- Opportunity to apply for seed grants from MAC ID
- Mentoring opportunity: to receive highly qualified trainees from McGill, or to send MAHEtrainees to McGill for specific skills/training
- Opportunity to participate in McGill Summer Institute courses
- Collaborate on MAC ID research projects and international grant proposals
- To learn about potential grant opportunities in the area of ID
- Members and their ID research will be showcased on the MAC ID website
- Conducting/ supporting infectious disease conference/training in Manipal/Mangalore campuses
- Conducting MAC ID international conference
- To apply for best MACID Faculty publication award

Opportunities for MAC ID Student members

- Students can participate in the MAC ID conference
- Students can organize any ID related CME/workshop/Quiz etc. under the supervision of any faculty who is a MAC ID member.
- To receive important and interesting ID related articles from MAC ID
- Opportunities to participate in MACID research projects
- Opportunity for best MAC ID student publication award

Manipal Centre for Infectious Diseases (MAC ID)

Prasanna School of Public Health

Manipal Academy of Higher Education, Manipal