APFCB News

The Newsletter of the Asia-Pacific Federation for Clinical Biochemistry and Laboratory Medicine for circulation among APFCB and IFCC members only

2024

Issue 2

Dr. Tan It Koon

Publication Team, 2024 Issue 2

Chief Editor	Prof. Pradeep Kumar Dabla, INDIA
Past Chief Editors	Dr. Raja Elina Raja Aziddin, MALAYSIA
	Prof. Praveen Sharma, INDIA
	Dr. Joseph B Lopez, MALAYSIA
Editorial Members	Dr. Leslie Lai, Kuala lumpur, MALAYSIA
	Prof. Ryunosuke Ohkawa, JAPAN
	Dr. Vivek Pant, NEPAL
	Prof. Deepak Parchwani, INDIA
	Dr. Mingma Lhamu Sherpa INDIA
	Dr. Alireza Lotfi Kian IRAN

APFCB Membership

Council Members

Australasian Association of Clinical Biochemists (AACB)
Association of Clinical Biochemists of India (ACBI)
Association for Clinical Biochemistry, Sri Lanka (ACBSL)
Chinese Society of Laboratory Medicine (CSLM)
Chinese Association for Clinical Biochemistry, Taiwan (CACB)
Hong Kong Society of Clinical Chemistry (HKSCC)
Indonesian Association for Clinical Chemistry (IACC)
Iranian Association of Clinical Laboratory Doctors (IACLD)
Japan Society of Clinical Chemistry (JSCC)
Korean Society of Clinical Chemistry (KSCC)
Malaysian Association of Clinical Biochemistry (MACB)
Mongolian Association of Health Laboratories (MAHL)
Nepal Association for Medical Laboratory Sciences (NAMLS)
Pakistan Society of Chemical Pathologists (PSCP)
Philippine Association of Medical Technologists (PAMET)
Singapore Association of Clinical Biochemistry (SACB)
Thailand Association of Clinical Biochemists (TACB)
Vietnamese Association of Clinical Biochemistry (VACB)

Affiliate Members

Chinese Association of Clinical Laboratory Management (CACLM)
Association of Medical Biochemists of India (AMBI)
Macao Laboratory Medicine Association (MLMA)
Nepalese Association for Clinical Chemistry (NACC)
College of Chemical Pathologists of Sri Lanka (CCPSL)
Philippine Council for Quality Assurance in Clinical Laboratories (PCQACL)

Corporate Members

Abbott Laboratories (Singapore) Pte Ltd.
Beckman Coulter Hong Kong Ltd.
Becton Dickinson Holdings Pte. Ltd.
Bio-Rad Laboratories (Singapore) Pte Ltd.
DiaSys Diagnostic Systems GmbH
Roche Diagnostics Asia Pacific Pte Ltd.
Siemens Healthcare Pte Ltd.
Snibe Diagnostics
Sukraa Software Solution Pvt Ltd.
Sysmex Corporation
RCPA QAP
Thermo Fisher Scientific
Waters Pacific
Greiner Bio-One Singapore Pte. Ltd.
Shenzhen Mindray Bio-Medical Electronics Co., Ltd.
QuidelOrtho

APFCB Executive Board and Chairmen of Committees, Elected 2024

Executive Board

President	Dr. Tony Badrick CEO, RCPAQAP Faculty of Health Sciences and Medicine, Bond University, Australia
Immediate Past President	Dr. Endang Hoyaranda Prodia Group, Jakarta, Indonesia
Vice-President	Dr. Samuel Vasikaran Consultant Chemical Pathologist, PathWest-Laboratory Medicine, Western Australia
Secretary	Prof. Praveen Sharma Former Professor and Head, Dean Research Biochemistry at AIIMS, Jodhpur, India Editor-in-chief, Indian Journal of Clinical Biochemistry
Treasurer	Dr. Raja Elina Raja Aziddin Senior Biochemist and Head of the Drug and Research Laboratory, Kuala Lumpur, Malaysia
Corporate Representative	Dr. Douglas W. Chung Area Marketing Manager Asia Pacific, Core Diagnostics at Abbott Laboratories

Chairman of Committees

Communications and Publications	Prof. Pradeep Kumar Dabla, INDIA
Education	Dr. Cui Wei, CHINA
Laboratory Management	Dr. Tjan Sian Hwa, INDONESIA
Scientific	Dr. Tze Ping Loh, SINGAPORE
Congress and Conference	Dr. Woei-horng Fang, TAIWAN

Submissions

The APFCB News welcomes suitable contributions for publication. These should be sent electronically to the Chief Editor. Statements of opinions are those of the contributors and are not to be construed as official statements, evaluations or endorsements by the APFCB or its official bodies.

Contact email: afpcbofficial@apfcb.org

Cover page: Dr. Tan It Koon, Clinical biochemist, artist, pianist, Renaissance man

Founding and Past President APFCB

Address

The registered address of APFCB is as follows:
APFCB, c/o Solid Track Management Pte Ltd. 150 Cecil Street, #10-06, Singapore 069543

Contents

From the desk of Chief Editor, APFCB eNews

Prof. Pradeep Kumar Dabla
Chief Editor, APFCB eNews

Dear Readers,

The APFCB Communication and Publication Committee (C-CP) has made significant progress in advancing the federation digital communication strategy. The committee has been instrumental in enhancing APFCB online presence, increasing engagement with member societies, and promoting the dissemination of valuable educational resources in laboratory medicine.

Key accomplishments include the development and maintenance of a dynamic APFCB website, which serves as a central hub for webinars, online courses, conferences, and scientific publications. Additionally, the C-CP revitalized APFCB social media presence on Facebook Twitter, LinkedIn, Instagram, and YouTube, significantly expanding its audience and improving engagement with national societies and clinical professionals worldwide.

The committee successfully registered the APFCB e-News with a Digital Object Identifier (DOI) and initiated the process for an International Standard Serial Number (ISSN), further enhancing the credibility and accessibility of its publications. The launch of the APFCB Webcast and e-Learning Programme has been another major milestone, promoting global learning and access to high-quality educational content. Thus, C-CP calls and invite member society members participation with online proposal submissions for webinars. Visit: https://www.apfcb.org/Webcast&e-Learning

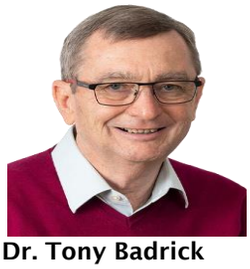
Looking forward, the C-CP aims to deepen stakeholder engagement by organizing virtual meetings, interactive sessions, and surveys to gather feedback. Plans also include diversifying content with special editions of APFCB News, increasing the use of video formats, and developing new digital tools, such as a mobile app, to enhance member experience and support APFCB mission of advancing clinical biochemistry and laboratory medicine.

Happy Reading!!

Best Wishes

Team APFCB C-CP

From the desk of APFCB President



Dr. Tony Badrick

President, APFCB

Dear Readers,

I thank you for your support of the hard work that goes into the preparation of this APFCB News. It provides a small link between us, showing we all have the same mindset and the same issues. The medical laboratory fraternity received recognition during COVID-19 from the community. It was clear that saving lives, livelihoods, and health systems depended on the processes we developed and our dedication and resilience. But people and governments have short memories as new challenges confront them. Many economies were almost broken by the pandemic, and the expenditures used to maintain the health system mean that governments need to reduce those costs now. As a result, we are starting to see governments asking for pathology services to reduce costs. This is not new for us, but our challenges have also increased. We know of the benefits that many new technologies in genomics and proteomics, PoCT, and self-testing devices can bring to our communities. But the introduction of these requires our input and management. We also must maintain all the current services.

The next challenge for us is to learn how to walk that tightrope of introducing new technologies into areas such as primary care and newborn screening while maintaining routine testing for disease screening and monitoring. This is not new but more pressing now as the expectations of our communities, health and citizens demand more, sooner. They are exposed to what is out there now because of the World Wide Web and social media. We also want to do the best we can, given the resources.

We may have always needed the support and wisdom of our broader scientific community as we question how we can face these issues.

The cornerstone of scientific progress is collective thought and communication. We challenge and test ideas, communicate the outcomes of adopting change, adopt our processes to continually improve our understanding of a problem, and solve it with this new community knowledge.

That is our challenge now. We all need to be part of the solution.

Best Wishes

President, APFCB

REPORT APFCB- COMMUNICATION AND PUBLICATIONS COMMITTEE (C-CP)

Prof (Dr.) Pradeep Kumar Dabla

Chair, APFCB C-CP

The Communication and Publication Committee (C-CP) of the Asia Pacific Federation of Clinical Biochemistry and Laboratory Medicine (APFCB) bears the critical responsibility of shaping, monitoring, and refining the organization's communication strategies and online presence. This committee plays an instrumental role in formulating and overseeing system-wide policies, ensuring that all digital operations align with the federation's overarching objectives. It also spearheads the online publication of APFCB News and collaborates closely with member associations and corporate partners to foster broader engagement and dissemination of valuable educational materials and resources to professionals in laboratory medicine. In doing so, the C-CP significantly contributes to the advancement of innovative ideas, guiding member associations in the development of policies and strategies that support the federation's mission of enhancing patient care.

Members of the APFCB C-CP for the 2023-2025 Term:

Chair: Dr. Pradeep Kumar Dabla

Web Editor: Dr. Deepak Parchwani

Social Media Coordinator: Dr. Vivek Pant

Dr. Ryunosuke Ohkawa

Dr. Mingma Lhamu Sherpa

Dr. Alireza Lotfi Kian

Members

Dr. Mayank Upadhyay (Corporate - QuidelOrtho)

Since the appointment of the current committee, the C-CP has taken proactive steps to enhance the federation's online visibility through the APFCB e-newsletter, social media platforms, and the official website. Over the past year, the committee has maintained robust communication channels and employed digital tools to promote the APFCB's activities across member societies within the Asia Pacific region and beyond, reaching countries affiliated with the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC).

Key Activities and Achievements:

1. **APFCB Website - Maintenance & Management:**
   The C-CP has overseen the creation, maintenance, and management of a new, dynamic APFCB website. This platform is regularly updated with the latest information on webinars, online courses, and virtual conferences hosted by APFCB, its member societies, and other international professional bodies. The website also features scientific publications, guidelines, and webinars (both live and recorded) on various topics of interest.

   Significant enhancements have been made to the website, including improved webinar visibility, the addition of a quick link tab for APFCB Auspices on the homepage, upgraded sections for announcements, social media integration, visitor statistics, and a dedicated space for corporate partners.

   The "APFCB Auspices Calendar" has been meticulously organized, reflecting the federation's commitment to fostering communication and information exchange in the field of laboratory medicine, which is essential for advancing patient care.

2. **Stewardship of APFCB Social Media Platforms:**
   Recognizing the pivotal role of social media in modern communication, the current C-CP has established new social media profiles and revitalized existing ones to effectively disseminate information regarding APFCB activities. The federation is now actively present on Facebook, Twitter, LinkedIn, Instagram, and YouTube, allowing it to reach a broader audience and engage more effectively with national societies and clinical laboratory professionals.

Social Media Links:

- Facebook: https://www.facebook.com/APFCB/
- Twitter: https://twitter.com/APFCB_LM
- Instagram: https://www.instagram.com/apfcb_lm/
- LinkedIn: https://www.linkedin.com/company/apfcb/
- YouTube: https://www.youtube.com/channel/UCoiicTsnVX-COjklgZHQ54Q

3. **Publication of Online Activities, Educational Materials, and Resources:**

   The C-CP has played a crucial role in the publication of online activities, educational materials, and resources, contributing to the creation of a vibrant and accessible learning ecosystem. By leveraging diverse digital platforms, the committee has facilitated the sharing of dynamic content, interactive exercises, and valuable resources, thereby promoting global access to education in laboratory medicine.

4. **Promotion of Educational and Federation Activities:**

   The C-CP has utilized the APFCB website and social media platforms to publicize upcoming events. Members are notified of impending events through blast emails, ensuring broad participation. The committee continues to diligently update and expand its member database to enhance communication and engagement.

5. **Publication of APFCB News:**

   The C-CP is responsible for the online publication of APFCB News, with the committee chair serving as the Chief Editor. In 2023, the newsletter was published twice, featuring a wealth of information, including annual reports from member societies, expert opinions on laboratory quality management and artificial intelligence, special reports on global medical lab celebrations, and sustainable green labs.

6. **DOI and ISSN Registration:**

   In the preceding year, the C-CP successfully completed the DOI (Digital Object Identifier) registration for the APFCB e-News. Additionally, the committee has initiated the ISSN (International Standard Serial Number) registration process, which is expected to be finalized in the coming weeks. These steps are crucial in enhancing the credibility and accessibility of the federation's publications.

7. **APFCB Webcast & e-Learning Programme:**

   The committee has launched the "APFCB Webcast & e-Learning Programme" as part of its efforts to promote global learning. This initiative is designed to provide accessible, high-quality educational content to laboratory professionals worldwide, furthering the federation's mission of advancing knowledge and practice in clinical biochemistry and laboratory medicine.

Future Recommendations:

- **Stakeholder Engagement:**
  - **Interactive Sessions with Member Associations:** To organize virtual meetings or interactive sessions with member associations to gather their input. This will help tailor content and initiatives to better meet the needs of the broader community.
  - **Survey and Feedback Mechanism:** To implement a survey or feedback mechanism to regularly gather input from stakeholders
- **Content Diversification:**
  - **Special Issues of APFCB News:** Publication of at least one special issue of the APFCB News focused on emerging topics in clinical biochemistry, such as advancements in AI, personalized medicine, or the role of laboratory medicine in global health crises.
  - **Incorporating Video Content:** To expand the use of video content, such as interviews with experts, laboratory tours, and recorded presentations, to engage a wider audience through various digital platforms.
- **Technology and Innovation:**
  - **Adoption of New Tools:** To adopt new digital tools and platforms that can enhance the APFCB's ability to produce and disseminate content, such as advanced analytics for social media, content management systems, or email marketing software, and anti-plagiarism software.
  - **Development of a Mobile App:** To develop an APFCB mobile app to provide members with easy access to publications, event information, and educational resources on the go.

Featuring Clinical Cases: The committee plans to feature more clinical cases in the upcoming issues of APFCB News, recognizing their value in medical education and the potential to inspire new ideas and approaches in the field.

As members of the Communication and Publication Committee, we remain committed to advancing the APFCB's mission and look forward to continuing our efforts to enhance communication, education, and collaboration within the global laboratory medicine community.

Report by:

Team APFCB C-CP

APFCB laboratory management committee (C-LM) - POCT Webinar

POCT Webinar Report (Organized by ACBI and APFCB C-LM), April 30, 2024

A webinar on "***Point-of-Care Testing***" was jointly organised by the Committee of Laboratory Management (C-LM), Asia Pacific Federation of Clinical Biochemistry and Laboratory Medicine (APFCB) and the Association of Clinical Biochemists of India (ACBI) on April 30, 2024 (1800 IST) through the Zoom-based ACBI eLearning platform under the auspices of the International Federation of Clinical Chemistry & Laboratory Medicine (IFCC) and APFCB.

The webinar was moderated by Dr Prasenjit Mitra, Assistant Professor, Department of Biochemistry, Postgraduate Institute of Medical Education & Research (PGIMER), Chandigarh, India who is also a member of APFCB C-LM.

There were three speakers in the event:

1. ***Dr Julie Shaw***: She is currently the Division Head for Biochemistry and POCT at The Ottawa Hospital and Eastern Ontario Regional Laboratories Association in Ottawa, Canada. She is also an Associate Professor in the Department of Pathology and Laboratory Medicine at the University of Ottawa. She chairs the POCT Special Interest Group of the Canadian Society of Clinical Chemists and is a corresponding member of the IFCC POCT working group.

2. ***Prof Adil Khan***: He is the Medical Director, Point-of-Care Testing & Clinical Chemistry in the Department of Pathology and Laboratory Medicine, Lewis Katz School of Medicine, Temple University, Philadelphia, USA. He is also the Chair of IFCC Committee on Point of Care Testing.

3. ***Dr Paloma Oliver Saez***: She is a Clinical Pathologist and the Point-of-Care Testing Coordinator in the Department of Laboratory Medicine, La Paz University Hospital, Madrid, Spain. She is also a member of the IFCC Committee on Point of Care Testing.

In the first talk of the webinar, Dr Julie Shaw highlighted the significance of Audits and Quality Indicator Monitoring for POCT. She discussed the essential components of quality assurance (QA) for POCT, which include device selection, verification, validation, training, certification, quality control (QC), proficiency testing, instrument comparisons, reagent lot validation, and

POCT Webinar Report (Organized by ACBI and APFCB C-LM), April 30, 2024

document control. QA for POCT can be divided into two categories: Controlling QA (e.g., POCT committee, lock-out testing) and Monitoring QA (e.g., QC, training, instrument audits, quality indicators). A good quality indicator is crucial for the testing process, as evidenced by risk assessment findings categorized into preanalytical (positive patient ID), analytical (quality control failures), and post-analytical (repeat of critical high results) stages. The presentation concluded by emphasizing the need for confirmation before clinical research, educating clinical staff on safe practices, taking precautions before testing, and managing risk assessment for critically high glucose repeats. While risk assessment is a good starting point for improvement, more readily available data-driven steps should also be monitored as quality indicators.

In the next presentation, Dr Adil Khan delved into the importance of professional training and certification in Point of Care Testing (POCT). He emphasized that POCT, often conducted outside clinical laboratories, should involve a wide range of health professionals, including trainees, paramedics, pharmacists, and clinicians. By providing comprehensive training and certification, the accuracy and effectiveness of POCT practices can be significantly improved. Reports from the International Federation of Chemistry (IFC) indicate that only 38% of related societies have a POCT committee, while 62% do not. Moreover, 55% of countries globally lack regulated POCT, leading to compromised healthcare in many regions. Thus, establishing quality coordinators or management teams to maintain standards is crucial, as demonstrated by the ADLM (AACC) in the US.

To develop a well-managed POCT committee, regulations at local or national levels are essential. These regulations should encompass personnel requirements, quality assurance, proficiency testing, detailed documentation, and frequent external audits. Additionally, focusing on pre-analytical, analytical, and post-analytical quality assurance can help eliminate errors and enhance accuracy. Training courses are vital for educating candidates on procedure manuals, specimen requirements, principles and protocols, safety precautions, test results, limitations, instrument selection and validation, and connectivity/IT protocols. This training is necessary to address inconsistencies arising from peer-to-peer training, where protocols might not be uniformly followed. Effective POCT practices require diverse training methods, including live and recorded lectures, manuals, posters, and regular assessments (practical, competitive, and written). Proper administration is needed to avoid operator incompetence and ensure adherence to training modules. Factors affecting accuracy, such as physiological variations, uncontrolled reagents/equipment, and environmental conditions (temperature and relative humidity), were also discussed. Comprehensive training and certification programs can educate health professionals on avoiding mistakes and implementing well-managed practices to enhance accuracy and improve results.

Dr Paloma Oliver, with 17 years of expertise, emphasized the role of a POC coordinator in ensuring efficient POCT practices. An experienced POC coordinator can manage workflow (pre-clinical, clinical, and post-clinical practices), test environments, and improve interpersonal and communication skills. Effective POCT management requires understanding the unit's status, clinical, operational, and economic outcomes, and making informed decisions. Thorough patient evaluations, proper sample collection, and the implementation of new testing procedures are crucial. Efforts should be made to ensure accurate method performance verification, procedure establishment, documentation, staff training, and competency in an error-free manner. Continuous training, internal and external quality assurance monitoring,

POCT Webinar Report (Organized by ACBI and APFCB C-LM), April 30, 2024

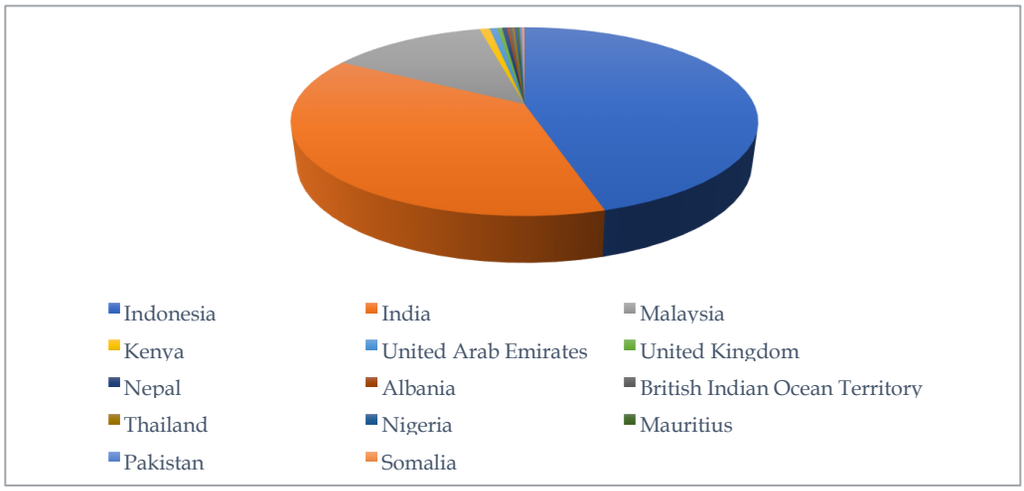
and daily personnel status checks are essential. Emphasis should also be placed on internal and external audits and collaborating on research projects with other institutions. In summary, professional training and certification in POCT are vital for improving accuracy and effectiveness. Establishing regulated POCT committees, providing comprehensive training, and ensuring continuous quality improvement are crucial steps towards better healthcare outcomes.

After the three presentations were over, Dr Prasenjit Mitra chaired a Q&A session. There were several questions that were asked by various participants. All the questions were answered by the three speakers. The Q&A session was extensive and interesting as it showed the interest of the participants in knowing about various aspects of POCT. Overall, it was a highly successful event with active participations from individuals across the globe. The participants provided their feedback through email about the impact the webinar had in their routine practise. There were suggestions to conduct more webinars on different aspects of POCT in the future.

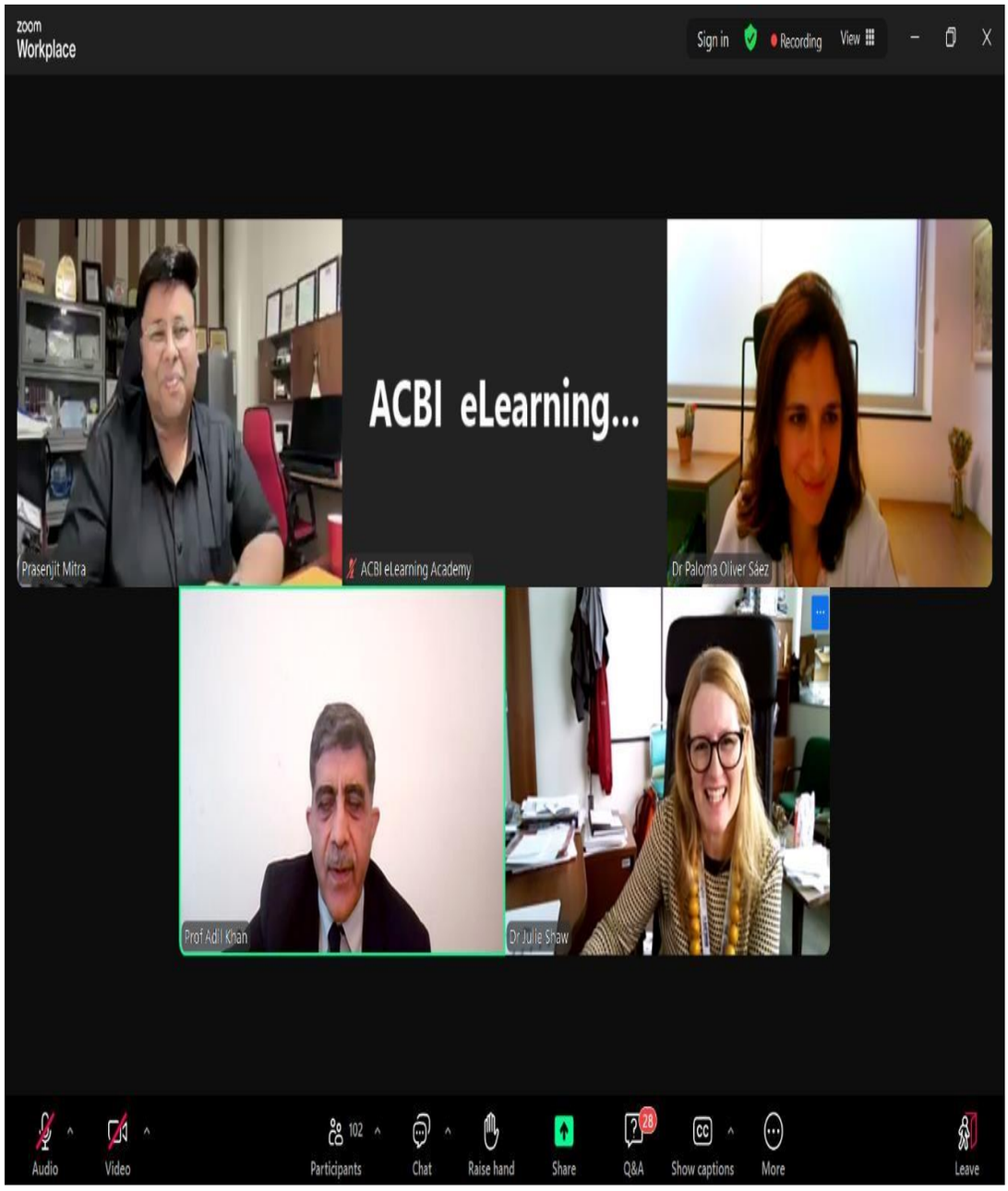
Attendee report:

Total participants: 485

Country Name	Count
Indonesia	220
India	184
Malaysia	63
Kenya	4
United Arab Emirates	3
United Kingdom	2
Nepal	2
Albania	1
British Indian Ocean Territory	1
Thailand	1
Nigeria	1
Mauritius	1
Pakistan	1
Somalia	1



POCT Webinar Report (Organized by ACBI and APFCB C-LM), April 30, 2024



Report prepared by
Dr Prasenjit Mitra
Member APFCB C-LM

OBITUARY

Dr. Tan It Koon

Clinical Biochemist, Artist, Pianist, Renaissance Man

by

Joseph Lopez

Past Chief Editor, APFCB News

Dr Tan It Koon, the founding President of the Singapore Association of Clinical Biochemists (SACB) and the APFCB, passed away on 1st May this year. Dr Tan was a pioneering clinical biochemist who loomed large in the Asia-Pacific region. During his lifetime, he served our profession with distinction and received acclaim as an artist, calligrapher and concert pianist.

Dr Tan graduated from the University of Singapore (now the National University of Singapore) with a First Class BSc Honours degree. He spent his entire professional life at the Department of Pathology of the Singapore General Hospital, where, as its Head, he managed its laboratory services, conducted training and undertook research. Dr Tan completed his PhD in Biochemistry in 1970 while working at the department and subsequently undertook post-doctoral studies in the United Kingdom and in the United States. In addition, he obtained professional qualifications in clinical biochemistry, these being the Mastership in Clinical Biochemistry (MCB), the Fellowship of the Royal College of Pathologists UK (FRCPath) and the Fellowship of the American Academy of Clinical Biochemistry (FACB).

In early 1991, at the request of the Singapore Government, he established a national reference laboratory for the investigation and diagnosis of inherited metabolic disorders. The results of the 13-year study in this area were shared at congresses and in publications. Later, at the request of the Deputy Prime Minister of his country, he authored a position paper on the value of Biotechnology in Singapore and organised an international Symposium on Biotechnology. These activities resulted in the establishment of the first Institute for Molecular and Cellular Biology (IMCB) in Singapore.

Dr Tan became a clinical biochemist just as the field was emerging as a profession in its own right. This led him to initiate the formation of the SACB, which he served as President for several years. With colleagues from Australia, he founded the APFCB, of which he was elected its first President. Together, they pioneered the APFCB congresses, with the first two held in Singapore, in 1979 and 1982. In his capacity as an APFCB office holder for many years, Dr Tan was also actively involved with the organisation of several subsequent congresses. He started the APFCB

Dr Tan became a clinical biochemist just as the field was emerging as a profession in its own right. This led him to initiate the formation of the SACB, which he served as President for several years. With colleagues from Australia, he founded the APFCB, of which he was elected its first President. Together, they pioneered the APFCB congresses, with the first two held in Singapore, in 1979 and 1982. In his capacity as an APFCB office holder for many years, Dr Tan was also actively involved with the organisation of several subsequent congresses. He started the APFCB News in 1983 and was its editor for many years.

Dr Tan was the first Asian to be elected to the IFCC Executive Board. As a WHO consultant and member of its various Expert Committees, he conducted educational training courses for clinical laboratory staff in the Asia-Pacific region. As a member of the Asian-Pacific Scientific Advisory Board of Becton Dickinson for over 10 years, he was involved in the publication of the BD Analyte Notes and the conduct of courses on pre- and non- analytical errors. He published more than 150 articles in local and international peer-reviewed journals, was a speaker or session chairman at various national and international conferences and served on the editorial board of several journals and books.

Dr Tan's innate talent in art and music became manifest in early childhood. His musical studies commenced under Singapore's most well-known music teachers, just before entering primary school. He was fortunate to be tutored throughout his secondary school and beyond by Singapore's first generation of artists who were recipients of the prestigious National Cultural Medallion Awards. Dr Tan gave his first public piano recital at the Victoria Memorial Hall, in Singapore, in 1957 and subsequently won top prizes for piano performances in 1959 and in the early 1960s. He was the winner of the Yamaha Singapore-Malaysia Music Composition Competition in mid-1970, where his winning composition was performed by the National Theatre Choir with him on the piano.

Dr Tan was an accomplished artist. His paintings during high school days won top awards at art exhibitions. He was invited to participate in the annual National Day art exhibitions organised by the Singapore Ministry of Culture from 1970. His more recent paintings accompanied with description, from the past decade and earlier, have appeared in the APFCB News and Clinical Chemistry. His outstanding achievements in the arts resulted in him being appointed by the Singapore Cabinet to the top management of the National Theatre Trust, a body dedicated to the promotion of cultural development and the performing arts.

Dr Tan spoke several Chinese dialects and languages. Even while he was busy working full-time in clinical biochemistry, his involvement with music, painting and calligraphy never ceased. He gave piano recitals at public concerts and private musical soirees. Even in his later years, he painted and practised his calligraphy and piano, often well into the night. In recent decades, his art works have been exhibited annually in Singapore and abroad. Dr Tan served as the President of the Southeast Asian Art Association and chaired its art exhibition organising committee for a number of years. He adjudicated the annual national level calligraphy competition for schools and tertiary institutions and was appointed adviser for promotion of cultural heritage and art at the Ngee Ann Corporation and Chaozhou Clan Association more than a decade ago. More recently, Dr Tan's profile and artworks earned him a chapter in each of four art books published in China featuring distinguished ethnic Chinese artists.

Dr Tan's immense contributions to the sciences and arts resulted in him being presented with two National Day Awards by the Government of Singapore and appointment to the Boards of the Cultural Foundation and Science Council of Singapore. Recognition by his peers in laboratory medicine came by way of international awards, including the inaugural APFCB Distinguished Service Award.

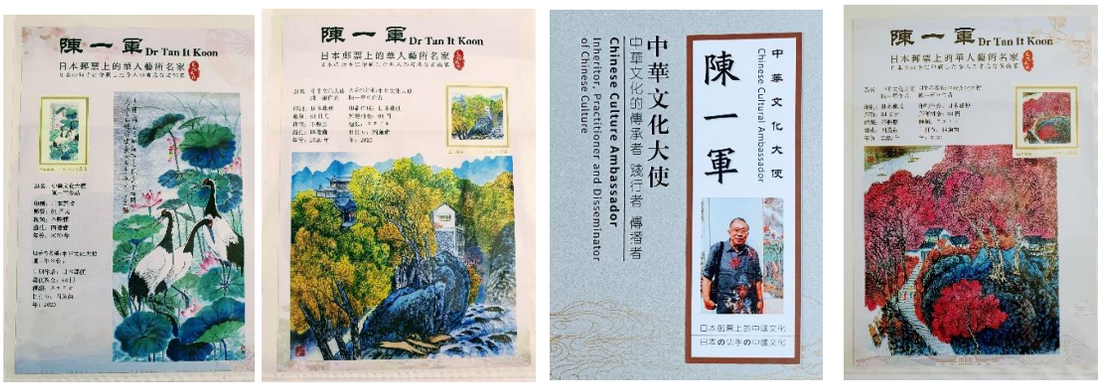
The European Renaissance from the 14th century to the 17th century was an intense period of cultural, artistic, political and economic flourish. Some of the greatest thinkers, authors, statesmen, scientists and artists in human history emerged during this era. The **Renaissance Man, a**n ideal which evolved from that time, recognised that the human kind had limitless capacities for development in multiple spheres of endeavour. The foremost embodiment of the **Renaissance Man** was perhaps Leonardo da Vinci, whose extraordinary gifts were manifest in the fields of art, science, music, invention and writing.

Dr Tan It Koon was a rare and exceptionally talented person**.** ***Requiescat in pace,*** Renaissance Man.

(*The writer is a founding member of the Malaysian ACB, a past President of the APFCB and a past member of the IFCC Executive Board who knew Dr Tan from the mid-1970s. We remained in touch until recently.)*

Three samples of Dr Tan It Koon's work in the arts:

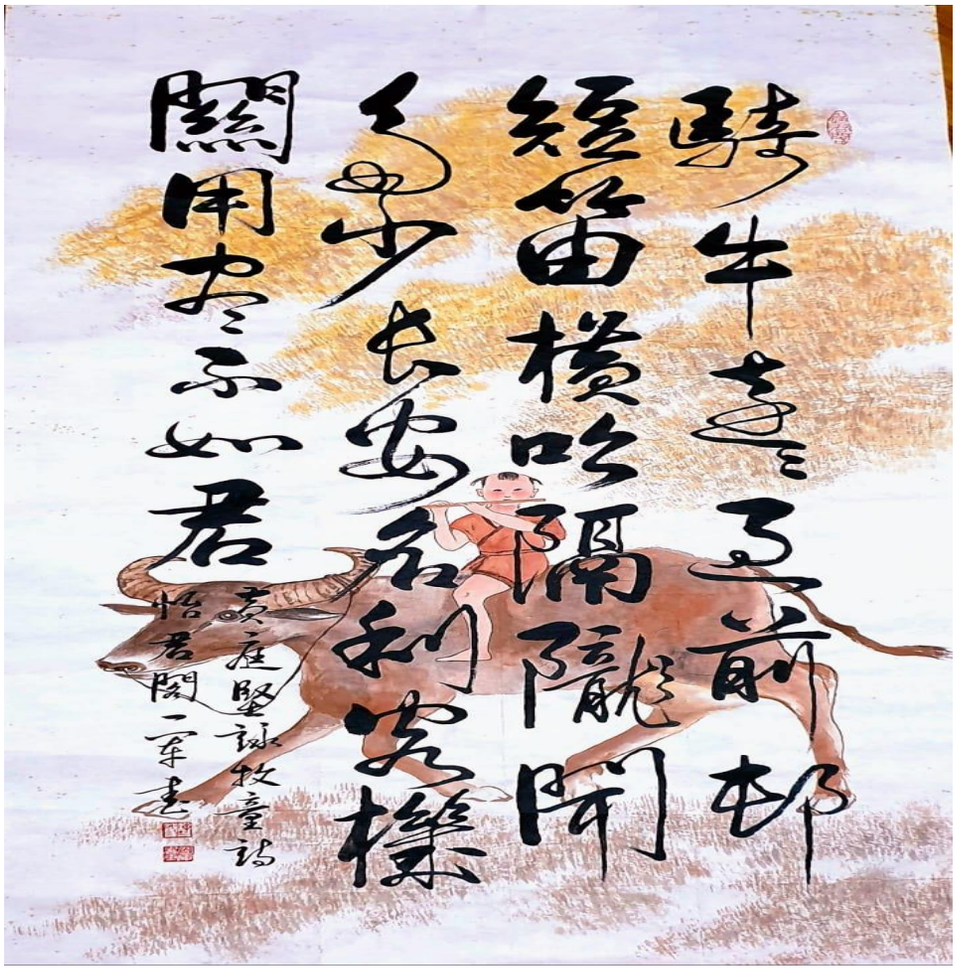
1. **Postage stamps** produced jointly by China and Japan to commemorate the 42nd Anniversary of Sino-Japan Peace, Cultural and Art Exchange Agreement, which featured a number of Dr Tan's artworks.



2. **A piano recital by Dr Tan** ***(https://youtu.be/-EHXRovfZCY)***

3. An example of Dr Tan's art and calligraphy with explanation

A 5-ft long ink-color Chinese brush painting combined with calligraphy by Dr Tan: ***"An Ox with a Young Cowherd Playing the Piccolo***** ". The inspiration for this painting came from the Song Dynasty poet (1045-1105) Huang Tingjian's "Poem of a Young Cowherd" that consisted of four sentences, each with seven words. It may be interpreted as follows: "A young cowherd riding on an ox passes a distant village. Sound of his piccolo playing could be heard drifting across the farm fields. Many famous and wealth-seeking people in the capital city of Changan spend too much time and effort in plotting schemes to bring them fame and fortune. How can they be compared with the cowherd who is so carefree and void of worry and stress? The poem in the artwork was written in the Running Script.

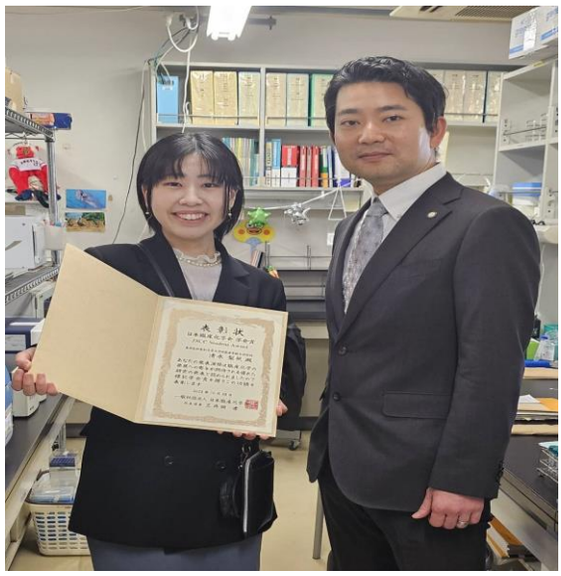


National Society Report- JSCC Japan

Japan Society of Clinical Chemistry (JSCC) launched the Student Award

Report by: Hideo Sakamoto, Ph.D. International Exchange Committee of JSCC

The Japan Society of Clinical Chemistry (JSCC) launched the Student Award from 2023. The JSCC Student Award is a prestigious recognition bestowed upon student members of the JSCC who have demonstrated remarkable research skills in the field of clinical chemistry. In 2023, total 25 students applied for the Student Award. As result, 10 students elected finalist and gave presentation on October 28th, 2023 at the Ochanomizu Sola City Conference Center, Tokyo, Japan. In this issue, we introduce four individuals who sent JSSC details of their research and aspirations to celebrate their activity.



From Left: Riho Shimizu (Award winner), Ryunosuke Ohkawa, Ph.D. (Mentor Professor)

Riho Shimizu (Tokyo Medical and Dental University, Department of Clinical Bioanalysis and Molecular Biology). Entitled with “Erythroid differentiation of K562 and analysis of its lipid transporter for investigation of red blood cells related lipid metabolism”. Serum cholesterol levels contained in lipoproteins are widely measured as biomarkers to predict a risk of atherosclerosis. However, red blood cells (RBCs) that occupy about half of blood by volume also have cholesterol abundantly in their membranes. The detailed mechanism of cholesterol metabolism in RBCs has not been fully cleared. They tried to establish a model cell for analyzing the metabolism in RBCs using human erythroleukemia K562 cells. I focused ATP-binding cassette transporter A1 (ABCA1), well-known as a cholesterol transporter, and found that ABCA1 was expressed on the erythroblast-liked cells differentiated from K562, and the expression was promoted using some chemical compounds. Functional analysis of the ABCA1 would be expected in future study.

She was inspired to this student symposium, which consisted of various themes. There was also a social gathering, and it was great to be able to interact with participants. She hopes they have an opportunity to communicate with each other again. She would like to express my gratitude to this award and do my best to aim for YIA next time.

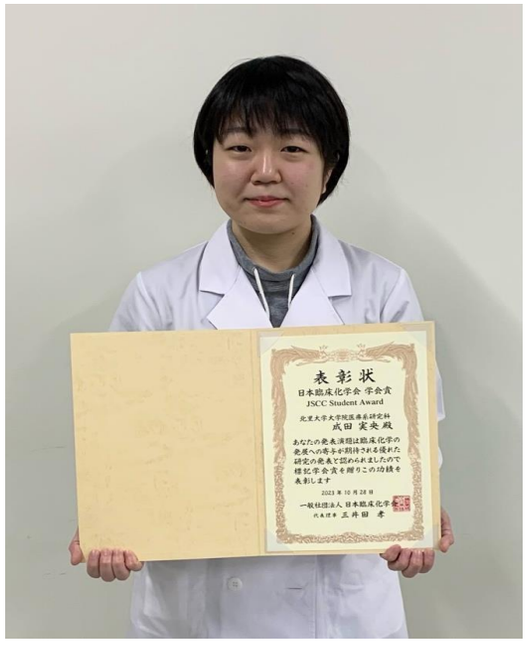
Hiroto Matsuura (Department of Clinical Laboratory Investigation, Graduate School of Medicine, Shinshu University. Entitled with “The effect of redox modification of apoE-Cys-thiol on the LRP1-mediated metabolism of apoE-containing lipoprotein metabolism”.

Hiroto Matsuura (Award winner)

The low-density lipoprotein (LDL) receptor-related protein (LRP) 1 participates in the metabolism of apolipoprotein (apo) E-containing lipoproteins (apoE-LP). They investigated the effects of modifications of cysteine (Cys)-thiol of apoE on LRP1-mediated metabolism. Among the three isoforms [E2 ($Cys^{112/158}$), E3 (Cys^{112}, Arg^{158}), E4 ($Arg^{112/158}$)], apoE2-LP exhibited the lowest affinity to LRP1 but were significantly catabolized, whereas apoE4-LP were sufficiently bound to LRP1 but showed the lowest catabolic capability. The reduction enhanced the binding and suppressed the catabolism of apoE3-LP, but had no effect on apoE2-LP. The formation of disulfide-linked complexes with apo AII suppressed binding, but enhanced the catabolism of apoE2-LP. Redox modifications of apoE-Cys-thiol may modulate the LRP1-mediated metabolism of apoE2- or apoE3-LP, but not apoE4-LP. The failure of this function may be involved in the pathophysiology of dyslipidemia. The current study offers a novel perspective on the physiological role of apoE in lipid metabolism. In addition, our findings are instrumental in understanding the pathology of various apoE-related diseases, including various atherosclerotic diseases and Alzheimer’s disease.

He is truly honored to receive the 2023 Japan Society of Clinical Chemistry (JSCC) student award. He would like to use this award as encouragement to continue my research activities.

Mio Narita (Graduate School of Medical Sciences, Kitasato University). Entitled with “Arachidonic acid-bound albumin induces cell proliferation and senescence via HIF-1α activation in proximal tubules".

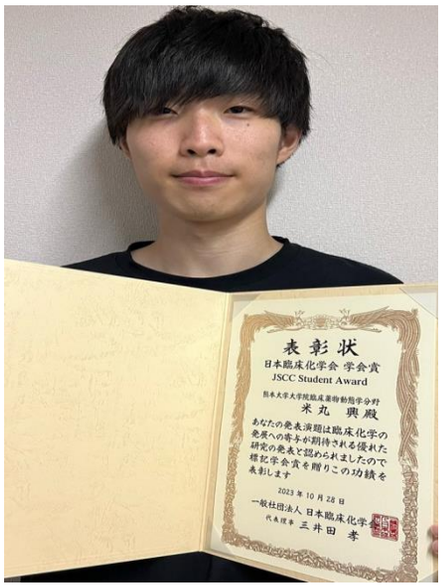


Mio Narita (Award winner)

Chronic kidney disease (CKD) is associated with senescence. Persistent proteinuria in CKD causes albumin overload in proximal tubular epithelial cells (PTECs). Moreover, fatty acid-bound albumin activates Hypoxic inducible factor (HIF)-1α. They observed that excessive albumin load causes cell proliferation and senescence in PTECs. However, the precise mechanism via which fatty acid-bound albumin induces cell proliferation and senescence remained unclear. Then they showed that fatty acid, especially arachidonic acid- bound albumin induces cell proliferation and senescence remained unclear. Then they showed that fatty acid, especially arachidonic acid-bound albumin, activated HIF-1α, which in turn induced cell proliferation and senescence. Additionally, HIF-1α activation induced dedifferentiation in the short term and was associated with abnormal fatty acid metabolism in the long term. Further research will be aimed at establishing the mechanism through which HIF-1α activation regulates CKD progression.

She is immensely grateful to Prof. Naohito Ishii, Dr. Yoshifumi Kurosaki, Dr. Akemi Imoto, and Dr. Naokazu Sato for their guidance. She trusts that this award will motivate me to continue researching with dedication.

Kou Yonemaru (Department of Clinical Pharmaceutical Sciences, Graduate School of Pharmaceutical Sciences, Kumamoto University). Entitled with “Establishing of novel therapies for tumor suppressor CYLD-negative and poor prognosis oral squamous cell carcinoma”.



Kou Yonemaru (Award winner)

Despite advances in early detection and multimodal treatment, the 5-year survival rate for patients with oral squamous cell carcinoma (OSCC) has not changed appreciably for the past 30 years due to the presence of treatment-resistant. Cylindromatosis (CYLD), a tumor suppressor, serves as a deubiquitinating enzyme and negatively regulates multiple cell-signaling pathways. Our previous studies have shown that loss of CYLD expression in OSCC tissues is significantly associated with poor prognosis of OSCC patients. Thus, he focused on CYLD expression in OSCC cells due to determine whether loss of CYLD expression is involved in cisplatin resistance, commonly used for OSCC, and elucidate its molecular mechanism. In this study, he found that cell survival rates in CYLD knockdown OSCC cells were significantly increased, indicating CYLD down-regulation caused the cisplatin resistance. Moreover, CYLD down-regulation induced the reduction of intracellular cisplatin accumulation ant the suppression of cisplatin-induced apoptosis via the NF-□B hyperactivation. Additionally, the combination of cisplatin and bortezomib, an NF-□B inhibitor, treatment exhibited significant anti-tumor effects on the cisplatin resistance caused by CYLD down-regulation. These findings suggest the possibilities that loss of CYLD expression may cause cisplatin resistance in OSCC patients through NF-□B hyperactivation and associated with poor prognosis in OSCC patients.
He is deeply honored to receive JSCC Student award at such a prestigious conference. This recognition is a testament of my entire research team. Looking ahead, He is committed to continuing his research and contributing to the treatment of OSCC patients.

National Society Report- KSCC Korea

Korean Society of Clinical Chemistry (KSCC)

KSCC Spring Meeting, April 11-12, 2024

KSCC held its spring meeting in Seoul on April 11-12, 2024. A total of 414 people attended the event, including 155 clinical pathologists, 36 resident doctors, 53 certified laboratory technologists, and others. The number of attendees increased compared to the previous spring meeting in 2023, which had 393 attendees. The meeting comprised five symposium sessions, two workshops, and an online education program.

During the symposium, we provided information on the latest laboratory tests and instruments in the field of clinical chemistry, covering Point-of-Care Testing quality management, guidelines for clinical performance evaluation, tests related to kidney diseases, thyroid hormone tests, and artificial intelligence-based laboratory operations. Furthermore, this spring meeting also placed emphasis on educational programs. A hands-on workshop on large-scale data analysis and a workshop on assay performance evaluation were held. Additionally, an online education program covering textbook material (Review Course) was delivered through a video-on-demand format.

Here are the details of the program and the event photos:

Symposium (April 12)

Time	Description	Speaker
09:00-09:10	**Opening**	
	Opening address	Yong Wha Lee (President, Korean Society of Clinical Chemistry, KSCC)
	Congratulatory address	Yunjung Cho (President, Korean Society for Laboratory Medicine, KSLM)
	Celebrating Excellence : Appreciation Recognition and Award Announcements	
09:10-10:40 (S1)	**Practical Aspects of POCT (Point-of-Care Testing) Quality Management**	**Chair: Gye Cheol Kwon (Chungnam National University, College of Medicine), Kyung Eun Song (Kyungpook National University School of Medicine)**
	Introduction and Management of New POCT Devices	Yoon Young Ahn (Soonchunhyang University College of Medicine)
	Managing Internal Quality Control Issues in Point-of-Care Testing	Kim Ha Nui (Korea University College of Medicin)
	Monitoring and User Training for POCT Quality Control	Sooin Choi (Soonchunhyang University College of Medicine)
10:40-11:10	**Exhibition**	
11:10-12:30 (S2)	**Guidelines for the Clinical Performance Evaluation of Clinical Chemistry Tests**	**Chair: Yeo-Min Yun (Konkuk University School of Medicine), Jehoon Lee (Catholic University of Korea, College of Medicine)**
	Revised Guidelines for Considerations in the Clinical Performance Study of In Vitro Diagnostic (IVD) Medical Devices	Sungjin Jo (Eunpyeong St. Mary's Hospital, Catholic University of Korea)
	Key Considerations in the Evaluation of Clinical Performance Study Data for In Vitro Diagnostic Medical Device Approval	Jina Kim (Division of In Vitro Diagnostic Devices National Institute of Food and Drug Safety Evaluation Ministry of Food and Drug Safety)
12:30-13:40	**Lunch, Exhibition**	

13:40-15:10 (S3)	**Updates on Clinical Chemistry Tests Related to Kidney Diseases**	**Chair: Hwan Sub Lim (Seoul Clinical Laboratories), Sail Chun (University of Ulsan College of Medicine)**
	A Nephrologist's View on Clinical Chemistry Tests for Kidney Diseases	Sang Youb Han (Inje University, Ilsan-Paik Hospital)
	Current Status of the Standardization of eGFR-Related Biomarkers in Korea	Tae-Dong Jeong (Ewha Womans University College of Medicine)
	Kidney Disease Lab Tests: You Might Want to Know	Rihwa Choi (Green Cross Laboratories)
15:10-15:40	**Exhibition**	
15:40-17:10 (S4)	**Recent Insights into Thyroid Hormone Tests**	**Chair: Soo-Youn Lee (Sungkyunkwan University School of Medicine), Eun-Hee Lee (Green Cross Laboratories)**
	Recent Clinical Practice Guidelines for Thyroid Diseases	Yonggeun Cho (Hallym University Sacred Heart Hospital)
	Standardization of Thyroid Hormone Tests	Sang-Guk Lee (Yonsei University College of Medicine)
	Analysis of Reference Intervals for Thyroid Hormone Tests	Sang Hoon Song (Seoul National University College of Medicine)

15:40-17:10 (S5)	**Current Status and Future Trends of Artificial Intelligence-Based Laboratory Operations**	**Chair: Min-Jeong Park (Hallym University College of Medicine), Pil Whan Park (Gachon University College of Medicine)**
	Artificial Intelligence in the Clinical Laboratory	Hangsik Shin (Asan Medical Center, University of Ulsan)
	Utilization of Large Language Models (LLMs) in the Laboratory	Kyu Tae Choi (Chungnam National University Sejong Hospital)
	Interpretation of Test Results Using Artificial Intelligence: An Example With Immunofixation Electrophoresis	Jun Hyung Lee (GC Labs)
17:10-17:30	**General Assembly and Closing Address**	

◎ Workshop A (April 11)

Time	Description	Speaker
09:00–12:00 / 14:00–17:00	Introduction	Hae-Il Park (Catholic University of Korea, College of Medicine)
	Basics underlying performance evaluation	Woochang Lee (University of Ulsan College of Medicine and Asan Medical Center)
	Evaluation and User Verification of Precision	Eun-Jung Cho (Hallym University College of Medicine)
	Evaluating and Establishing the Linearity Interval and Extended Measuring Interval	Jooyoung Cho (Yonsei University Wonju College of Medicine)

◎ Workshop B (April 12)

Time	Description	Speaker
13:40–15:10	Getting Started with Large-scale Data Analysis	Won-Ki Min (SD BIOSENSOR)

◎ Review Course (VOD)

Screening date	Description	Speaker
April 13, 2024–May 10, 2024	**General Clinical Chemistry**	
	The Basics of Clinical Performance Evaluation for Measurement Procedures: Precision	Eun-jung Cho (Hallym University College of Medicine)
	Risk Management-Based Quality Control in the Clinical Laboratory	Minje Han (Kangdong Sacred Heart Hospital, Hallym University)
	Major Interfering Factors in Clinical Chemistry Tests	Jaewoo Chung (Dongguk University, Ilsan Hospital)
	Special Clinical Chemistry	
	Urine Analysis: Dipstick and Sediment Examination	Sollip Kim (University of Ulsan College of Medicine, Asan Medical Center)
	Myocardial Injury Biomarkers	Moon Soo Young (Eone Laboratories)
	Heart Failure Biomarkers	Hanwool Cho (Catholic University of Korea, St. Vincent's Hospital)
	Clinical Applications of Cardiovascular Biomarkers	Youngwoo Jang (Gachon University, Gil Medical Center)

Professor Yong Wha Lee (President of KSCC) delivering the opening address

Executive board members and advisors of KSCC

The organizing committee of the 2024 KSCC spring meeting

KSCC 2024 Fall Meeting Plan

KSCC will hold the fall meeting in Seoul on October 16-17, 2024.

National Society Report- SACB, Singapore

NAME OF SOCIETY	Singapore Association of Clinical Biochemists (SACB)
President (APFCB Representative)	Dr Leslie Lam
Vice-President	Mr Johnson Setoh
Treasurer	Dr Tan Jun Guan
Secretary	Dr Kho Shu Hui
Assistant Secretary	Ms Chong Ai Teng
Council Members	Ms Joanne Lee Ms Ummi Kulsum Ms Siti Ramlah
Co-opted members	Dr Shaun Tan Ms Andrea Goh Ms Violet Lee Ms Ho Mun Jun

ANNUAL SCIENTIFIC MEETING AND ANNUAL GENERAL MEETING 2024

The Singapore Association of Clinical Biochemists (SACB) held its Annual Scientific Meeting (ASM) and Annual General Meeting (AGM) on 2nd March 2024 at M Hotel Singapore. It was an annual event attended by over 200 delegates and supported by 13 industry partners. The event was opened by the 4th President of SACB, Dr Leslie Lam followed by a plenary lecture and two concurrent sessions throughout the day. The AGM also took place during the day where SACB financial report and activities held during the previous year were shared with SACB members. Election of council members took place during the 46th AGM and new council members were elected. A Promotion ceremony for Associate members to Professional members was held for members who have at least 3 years of working experience in a clinical laboratory and have been a SACB associate member for 3 consecutive years. Several industry partners also set up booths on that day and showcased their products to delegates.

Figure 1 SACB Tote Bag

Figure 2 SACB Council Members 2024-2026

The scientific symposium featured the following topics and speakers:

- Primary Aldosteronism (PA) - A Neglected Cause of Hypertension. Advancement in Diagnostic Capability through Rapid Screening test for PA by Ms Andrea Goh (Regional Product & Marketing Manager, APAC-Export Diasorin APAC)
- POCT Compliance by Mr Duncan Mills (AegisPOC)
- Digital Health Horizons: Clinical Decision Support for Healthier Aging by Mr Arpit Onawale (APAC Digital Health Solutions Director Abbott Laboratories)
- The Technological Evolution in Blood Gas Analysis by Mr Davide Colombo (Global Acute Care Expert Werfen)
- From Gels to Mechanical Barriers: The Evolution of Blood Collection Tube Barrier Technology by Dr Pearline Teo (Associate Director Medical Affairs, Integrated Diagnostic Solutions Becton Dickinson)
- Beta-trace Protein: One Biomarker, Two Clinical Needs by Ms Aya Tan (Assay and Clinical Marketing Manager, Laboratory Solutions Siemens Healthineers)
- Anaemia Management in Laboratory Settings by Dr Wendy Phua (Scientific Affairs Liaison, Sysmex Asia Pacific).

Figure 3 SACB members listening attentively to ASM symposium

SACB EDUCATION PROGRAMME 2023

SACB also held its annual ten-weekly education programme series every Wednesday from 6th September 2023 to 8th November 2023 via hybrid mode. SACB received 191 sign-ups for this annual event. The topics and speakers are listed as follows:

Date	Topic	Speaker
6 Sep	How To Interpret Renal Function Tests	Dr Michael Lau Registrar Changi General Hospital
13 Sep	Clinical Case Studies	Prof Aw Tar Choon Senior Consultant Changi General Hospital
20 Sep	How To Determine Reference Intervals	Dr Tan Jun Guan Associate Consultant Khoo Teck Puat Hospital
27 Sep	How To Interpret Thyroid Function Tests	Dr Lim Ming Hwee Registrar Singapore General Hospital
4 Oct	How To Troubleshoot EQA	Ms Pallavi Chincholkar Deputy Manager Parkway Laboratories
11 Oct	How To Evaluate Qualitative & Semi-quantitative Assays	A/Prof Robert Hawkins Senior Consultant Tan Tock Seng Hospital
18 Oct	How To Perform QC Troubleshooting & Periodic QC Review	Ms Erin Choo Senior Medical Technologist Parkway Laboratories
25 Oct	How To Perform Urinalysis	Mr Johnson Setoh Principal Medical Laboratory Scientist Sengkang General Hospital

1 Nov	How To Interpret Blood Gases	Dr Shaun Tan Associate Consultant National University Hospital
8 Nov	How To Prevent Validating Non-sensical Lab Results	Ms Joanne Lee Senior Manager Parkway Laboratories

SACB EDUSERIES 2023-2024

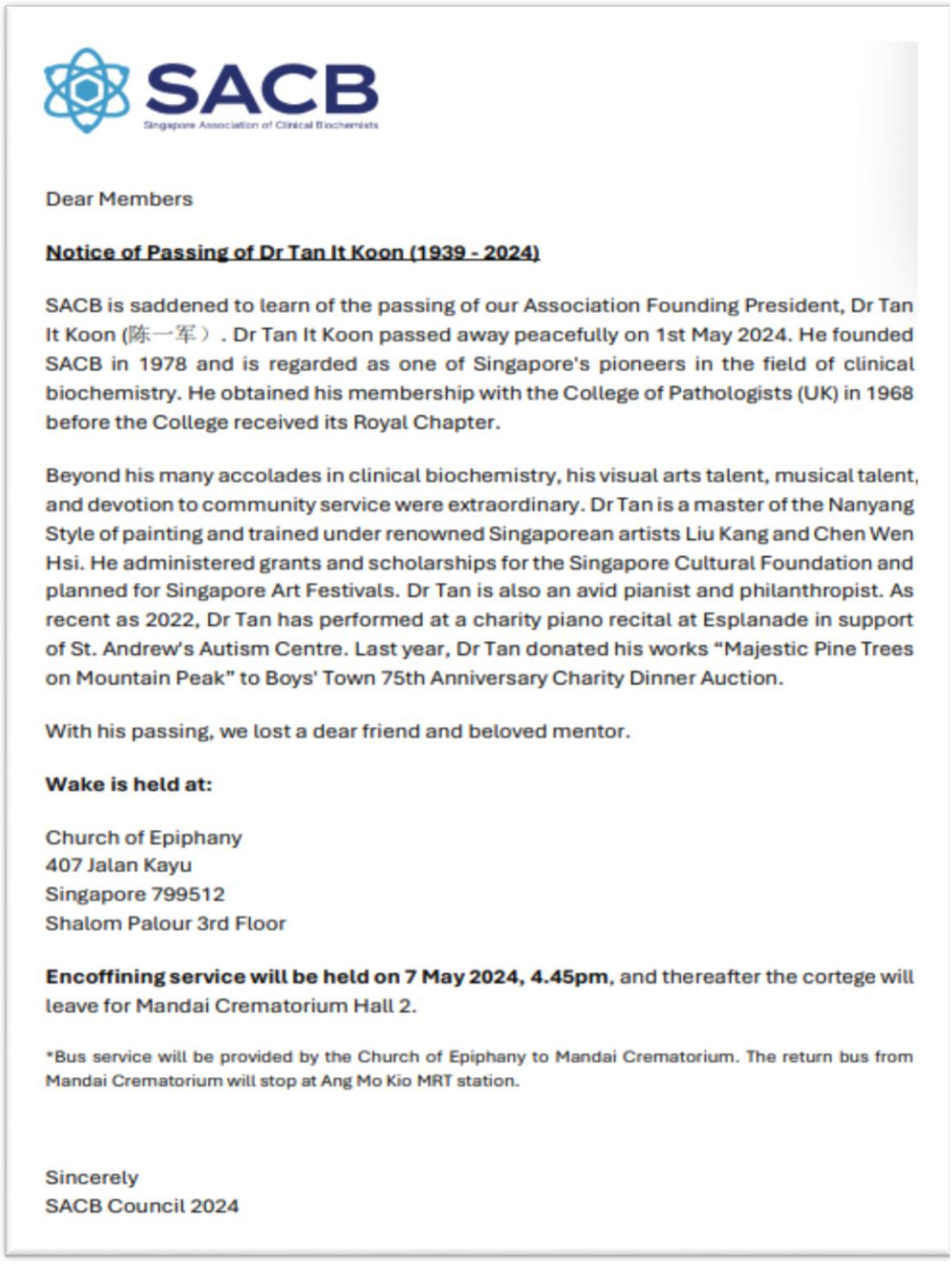
SACB, supported by various industry partners also organised bi-monthly Evening Eduseries where invited speakers shared new and upcoming assays and practices in the laboratory arena. Attendees were also treated with sumptuous dinner kindly sponsored by our industry partners before the event. The topics are as follows:

Date	Topic	Sponsor
11 May 2023	Pre-analytical interferences and Coagulation Result interpretation	Sysmex Asia Pacific
13 July 2023	Managing Lot-to-Lot Variability	Abbott Diagnostics
12 Sep 2023	Understanding Haemolysis, Icterus and Lipaemia: Impacts on Laboratory Testing and Patient Diagnoses	Siemens Healthineers
30 Nov 2023	Hb Variants and its effects on HbA1c, Quality Assurance: Assuring Reliability of HbA1c results	Bio-Rad Laboratories
23 Jan 2024	ABCs of Pre-eclampsia	Roche Diagnostics
15 April 2024	Blood-based biomarkers for early cancer detection & Patient Blood Management and Sample Volume Control	Greiner Bio-One
15 June 2024	Primary Aldosteronism: The challenge in screening and diagnosis	Diasorin

Greiner also kindly co-hosted a Scientific Workshop with SACB on 16 April 2024. The workshop was conducted by Prof Ana-Maria Simundic (Director Global Department Medical and Clinical Affairs, Greiner Bio-One).

PASSING OF DR TAN IT KOON

On a sad note, SACB received news on the passing of our founding President, Dr Tan It Koon in May 2024. A wreath was sent to the funeral and notice was sent to all members on his passing and highlighting his contributions to Clinical Biochemistry and the community. With his passing, we lost a dear friend and beloved mentor!



SACB
Singapore Association of Clinical Biochemists

Dear Members

Notice of Passing of Dr Tan It Koon (1939 - 2024)

SACB is saddened to learn of the passing of our Association Founding President, Dr Tan It Koon (陈一军）. Dr Tan It Koon passed away peacefully on 1st May 2024. He founded SACB in 1978 and is regarded as one of Singapore's pioneers in the field of clinical biochemistry. He obtained his membership with the College of Pathologists (UK) in 1968 before the College received its Royal Chapter.

Beyond his many accolades in clinical biochemistry, his visual arts talent, musical talent, and devotion to community service were extraordinary. Dr Tan is a master of the Nanyang Style of painting and trained under renowned Singaporean artists Liu Kang and Chen Wen Hsi. He administered grants and scholarships for the Singapore Cultural Foundation and planned for Singapore Art Festivals. Dr Tan is also an avid pianist and philanthropist. As recent as 2022, Dr Tan has performed at a charity piano recital at Esplanade in support of St. Andrew's Autism Centre. Last year, Dr Tan donated his works "Majestic Pine Trees on Mountain Peak" to Boys' Town 75th Anniversary Charity Dinner Auction.

With his passing, we lost a dear friend and beloved mentor.

Wake is held at:

Church of Epiphany
407 Jalan Kayu
Singapore 799512
Shalom Palour 3rd Floor

Encoffining service will be held on 7 May 2024, 4.45pm, and thereafter the cortege will leave for Mandai Crematorium Hall 2.

*Bus service will be provided by the Church of Epiphany to Mandai Crematorium. The return bus from Mandai Crematorium will stop at Ang Mo Kio MRT station.

Sincerely
SACB Council 2024

Figure 4 Notice on Dr Tan It Koon's passing to SACB members

National Society Report- ACBI India

ASSOCIATION OF CLINICAL BIOCHEMISTS OF INDIA

FORTHCOMING EVENT FOR 2024:

This year the Annual National Conference will be held in Chandigarh, organized by the Department of Biochemistry, PGIMER, and Chandigarh from 4th to 6th December 2024.

Dear Colleagues,

On behalf of the Organizing Committee, we extend a warm welcome to the picturesque city of Chandigarh for the 50th Annual Conference of the Association of Clinical Biochemists of India (ACBICON 2024), scheduled to take place from December 4th to 7th 2024 at Hotel Mount View, Chandigarh. The conference is being organized by the Department of Biochemistry, PGIMER, and Chandigarh.

The theme of the conference is "From Laboratory to Life: Recent Advances in Basic and Medical Research for Global Healthcare".

Chandigarh, renowned for its urban design, vibrant culture, lively markets, and the spirited nature of its inhabitants, eagerly awaits your presence. The city is famous for attractions such as Nek Chand's Rock Garden, Sukhna Lake, numerous beautiful gardens, shopping malls, and food courts. Chandigarh enjoys excellent connectivity by air, rail, and road to all major cities in India. Nestled at the foothills of the Shivalik range of the Himalayas, Chandigarh, known as the "City Beautiful" serves as a gateway to nearby hill stations and is in close proximity to the famous 'Golden Temple' of Amritsar.

The Scientific Committee is honoured to host distinguished speakers from India and around the world, providing a truly global perspective to the meeting. The 50th ACBICON 2024 conference offers an excellent opportunity to stay updated on the latest advances and network with peers from across the country and the globe. The organizing committee is dedicated to ensure that the conference becomes an academically and culturally enriching experience for all the attendees.

We eagerly anticipate your participation in the Conference.

Thanks and best regards,

Prof. Indu Verma
Department of Biochemistry,
Research Block-A, PGIMER, Sector 12, Chandigarh 160012
Email id:- acbicon2024@gmail.com
Mob:- +91 85952 51325

Scientific activities held in different parts of the country under ACBI banner:

ACBICON-Odisha 2024 REPORT

The Department of Biochemistry AIIMS Bhubaneswar, conducted the Second State Chapter conference of the Association of Clinical Biochemists of Odisha (ACBI) on "Transforming Trends in Cardiac Health", on the 16th March 2024.

The program was inaugurated by Prof P. R Mahapatra, Dean (Academics) and Officiating Director. Prof Dilip Kumar Parida, Medical Superintendent AIIMS Bhubaneswar and Prof Kannan Vaidyanathan, President ACBI also graced the inauguration event, which started with lamp-lighting and welcome address by Prof Manaswini Mangaraj, Head of the Department of Biochemistry, AIIMS Bhubaneswar and Organizing Chairperson of the conference. Dr Debapriya Bandyopadhyay, Organizing Secretary proposed the vote of thanks.

There were three scientific sessions during the conference.

The first scientific session was under the chairmanship of Prof Pramila Kumari Mishra, Head, Department of Biochemistry, Hi-Tech Medical College and Hospital, Bhubaneswar & Prof Pranati Nanda, Head , Department of Physiology, AIIMS, Bhubaneswar. There were two lectures. First one on "Insights into Cardiac metabolism" by Prof Subir Das, Head, Department of Biochemistry, JNM Medical College, Kalyani, West Bengal and the second on "Myocardial Ischaemia in Young" by Dr Prasant Kumar Sahoo, Senior Consultant & Interventional Cardiologist, Apollo Hospital, Bhubaneswar.

The second scientific session was under the chairmanship of Prof Pratima Kumari Sahu, Head, Department of Biochemistry, SCB Medical College and Hospital, Cuttack and Prof Suchismita Panda, Head, Department of Biochemistry, DD Medical College and Hospital, Keonjhar. There were two lectures. First on "Covid 19 Aftermath-Impact on cardiac health" by Dr Saroj Kumar Sahoo, Assistant Professor, Department of Cardiology, AIIMS, Bhubaneswar and the second lecture on "Novel cardiac biomarkers in Diagnosis & Prognosis of Cardiac Health" by Prof Kannan Vaidyanathan, President ACBI and Head, Department of Biochemistry, Believer's Church Medical College Thiruvalla, Kerala.

The post-lunch third scientific session was under the chairmanship of Prof Manisha R Gaikwad, Head, Department of Anatomy, AIIMS, Bhubaneswar & Prof Rachita Nanda, Department of Biochemistry, AIIMS, Raipur. The session started with a deliberation on "Reperfusion Injury" by Dr. Soumya Ranjan Mahapatra, Associate Professor, Department of Cardiology, IMS & SUM Hospital, Bhubaneswar, followed by a talk on "Relevance of Statins in Clinical scenario" by Dr Dipak Ranjan Das, Associate Professor, Department of Cardiology, SCB Medical College and Hospital, Cuttack.

After a tea break, the Scientific Paper Presentations for the post-graduate students was conducted by Dr Gautom Kumar Saharia, Scientific Convener. The event was judged by Prof Dr Subir Das, Head, Department of Biochemistry, JNM Medical College, Kalyani, West Bengal and Prof Dr Sucharita Mohanty, Head, Department of Biochemistry, BB Medical College and Hospital, Balangir. The first prize was bagged by Dr.Srimayee Mahapatra , Department of Biochemistry, SCBMCH, Cuttack .The second prize was won by Dr K Farzia, Department of Biochemistry, AIIMS, Bhubaneswar and third prize went to Dr Aswin K Nair , Department of Physiology, AIIMS, Bhubaneswar.

There were around 80 registered delegates from various medical colleges of Odisha for this conference.

The program was coordinated by Dr Tina Das, Assistant Professor, Department of Biochemistry, AIIMS, Bhubaneswar.

Dr Prakruti Dash, Co-organizing Secretary, Dr.Ramadass Balamurugan, Additional Professor and Dr Suchitra Kumari Additional Professor along with PG students, SRs and staff of Department of Biochemistry were instrumental in organizing the event successfully.

The Odisha Council for Medical Registration (OCMR) has awarded 4 credit points for the attendees.

The Dignitaries on the Dais

Prof Dr Manaswini Mangaraj, Organizing Chairperson

Group photo with all delegates

Central Zone Conference

The **Central Zone Conference of the Association of Clinical Biochemists of India (CZACBICON 2024)** was held at the AIIMS Bhopal, from **19th to 20th January, 2024**, on the theme **"Innovations in Clinical Biochemistry".** It was organised by the Department of Biochemistry, AIIMS Bhopal, India. Prof. (Dr.) Ajay Singh, Executive Director, AIIMS, Bhopal, inaugurated the conference and expressed his views on this occasion. Prof. (Dr.) Jagat R Kanwar, Head, Department of Biochemistry, AIIMS, Bhopal also threw light on the theme of this conference while welcoming the conference participants. An inspiring and enlightening scientific program was prepared by the scientific committee of CZACBICON 2024. The scientific session started with the theme of Innovation in Clinical Biochemistry and applications in health care. Extensive educative sessions were conducted by well-known national speakers. The keynote speaker of the session was Prof. (Dr.) D M Vasudevan. Other speakers were Prof. (Dr.) Kannan Vaidyanathan, Prof. (Dr.) Subir Kumar Das, Dr. K G Raghu, Dr. Bhawna Bhimte, Dr. Mithun Roy, and Dr. Priyadip Das. More than 70 learned professionals shared their knowledge about recent advances and technologies in the field of Clinical Biochemistry through oral and poster presentations. The conference was attended by over 150 delegates from all over the India. Three recent techniques oriented state-of-the-art preconference workshops were also held on the 19th of January, 2024. These workshops on***: a. Next Generation Sequencing b. Inborn Metabolic Disorder c. Diagnosis of Monoclonal Gammopathies*** were highly informative and rigorous and were concluded with an interactive question- answer session with the participants. The vote of thanks was given by Dr. Sukhes Mukherjee, Organising Secretory, CZACBICON 2024. He extended gratitude to all the attendees and highlighted the importance of the event.

North Zone conference

The North Zone conference of Association of Clinical Biochemists of India was held successfully on 1st & 2nd February 2024 at All India Institute of Medical Sciences, Jodhpur. The conference was organized by Department of Biochemistry, All India Institute of Medical Sciences, Jodhpur with theme of "Biochemistry: Basics to Translational". Dr. Dharmveer Yadav (Organizing Secretary), said that the event aimed to create a platform for collaboration and networking within the field of Biochemistry. The conference brought together experts, researchers, and professionals from Biochemistry and related specialties to exchange knowledge, share insights, and discuss recent advancements in translational applications of biochemistry.

The conference featured three different workshops on 31st January, 2024. The workshops allowed participants to get exposure on Genetic Analyzer, Basic molecular techniques and Best practices in Phlebotomy. Around 50 participants attended the workshop.

The conference on 1st & 2nd February 2024 was attended by renowned speakers from academia and industry which led to insightful discussions, providing valuable takeaways for attendees.

The Inaugural ceremony was conducted on 2nd February 2024 and was occasion was graced by Dr. S.S.Agarwal , President, AIIMS Jodhpur, Prof. Dr. Madhabananda Kar, Executive Director, AIIMS Jodhpur. Dr. Praveen Sharma, President RSACBI, Dr. Rajiv Ranjan Sinha, General Secretary, ACBI and Dr.Mithu Banerjee,Organising Chairperson(HOD Biocheistry,AIIMS Jodhpur). As part of social responsibility, the ceremony was followed by cultural programme by talented children from Lakshya Bal Punrwas Kendra, Osian.

Three parallel sessions were conducted on 1st & 2nd February 2024 which discussed cutting edge research in the fields of Interdisciplinary research, Laboratory Medicine, Molecular Biology, Diabetes, Integrative Health, Neurodegeneration, Therapeutic and traditional medicine and Tumor.

An Interactive panel discussion was conducted on reference interval estimation which provided a forum for experts to delve into a critical issues faced by diagnostic medicine. Attendees actively participated, contributing to vibrant and informative conversations.

A dedicated poster session provided an opportunity for researchers and students to present their work in a visual format. This fostered discussions and allowed for one-on-one interactions with presenters. A concurrent industry exhibition showcased cutting-edge products, services, and technologies from leading companies in the Diagnostics. Attendees had the chance to explore and engage with exhibitors, gaining insights into the latest advancements.

The conference attracted a 250+ diverse audience, including professionals, researchers, academics, and students from around the country. The interactive nature of the sessions and the quality of presentations ensured active participation and engagement throughout the event.






NORTH ZONE ACBI
CONFERENCE 2024

NORTH ZONE ACBI
CONFERENCE 2024

IMMUNOMEET 2024 – West Bengal

Department of Biochemistry, College of Medicine & JNM Hospital, WBUHS organized an outreach Conference "Immunomeet" covering immunesystem and immunodiagnostics at Baranti Village Resort, Baranti, Purulia, West Bengal on March 27-29, 2024. This academic meet was jointly supported by Association of Clinical Biochemists of India (ACBI), Indian Immunology Society (IIS), Indian Immunology Foundation (IIF). Dr Amitabha Das, Associate Professor of Biochemistry, COMJNMH welcome the delegates. Prof Krishnajyoti Goswami, past-President of ACBI, addressed the delegates. All senior members inaugurated the program with lamp lighting. Dr Vijay K Kutala from Nizam's Institute of Medical Sciences (NIMS), Hyderabad released the Abstract book and Souvenir.

Dr Dablu Lal Gupta, Assistant Professor from AIIMS, Raipur discussed about the mutations in the RBD domain at the residues K417, E484, and N501 that reduced the immuno-reactivity with antisera obtained from vaccinated people and SARS-COV-2 recovered patients. Prof. Dibyajyoti Banerjee from PGIMER, Chandigarh had established that Vitamin D and some of the related molecules (analogs and other steroids) bind with the ACE2 receptor. In case the Vitamin D-associated molecules bind with more affinity than the SARS-CoV-2 proteins then inhalation supplementation of such molecules will not allow the pathogen to bind with the ACE2 receptor thus imparting a host-based prevention mode.

Dr Amit Pal from AIIMS, Kalyani discussed about the role of selenium levels in colorectal cancer. Dr. Sanchayan Sinha from College of Medicine and Sagore Dutta Hospital, Kolkata reported three cases of dengue in pediatric and adolescent age groups, with myositis presenting as muscle weakness. Dr Lalthanzami Sailo from COMJNMH, Kalyani, discussed on the role of serum TGF-β1 and hydroxyproline in female uterine prolapse. Sharmila Wahengbam and Romabai Chanu from NIT, Manipur described the combined chemotherapeutic effect by bimetallic cobalt (III) and platinum (II) complexes. Gobinda Bag from NIT, Manipur developed red-light activable oxovanadium (IV) complexes that enhanced therapeutic activity on photo-activation through the singlet oxygen generation making the prodrug system remarkably cytotoxic against cancer cells.

Small molecules like antibiotics are widely used as therapeutic agents against diseases and also detectable marker for diseases. Dr. Rajasri Bhattacharyya from PGIMER, Chandigarh have identified peptide as diagnostic and therapeutic marker against diseases. Sruti E from TRIHMS, Arunachal Pradesh investigated the role of insulin resistance and serum TNF-α level in overweight, obese with and without metabolic syndrome and their risk for cancer. Dr. Tapan Mondal from COMJNMH, Kalyani, identified the role of serum Mg^{2+}, erythrocytic $Na^{+}K^{+}$ATPase and insulin resistance with any possible association in between them in case of type 2 diabetes mellitus.

Complement is a pro-inflammatory system comprising of soluble and membrane bound proteins. Their importance in several disorders is increasingly being realized. In this context, a detailed presentations by 2nd year MBBS students on Complement system was enjoyed and

applauded by every delegate. Prof. Nibhriti Das from AIIMS, New Delhi discussed on the complement regulatory proteins as biomarkers. She explored the disease association and potential of leucocyte DAF (Decay Accelerating Factor) and Membrane Cofactor Protein (MCP) as biomarkers for rheumatoid arthritis and for that, investigated the disease related modulation of these two vital transmembrane complement regulators.

Chikungunya is a viral disease caused by positive sense single stranded RNA virus. This virus transmitted to human by Aedes misquotes. High fever, myaligia, Joint swelling, body rashes are characteristic features of Chikungunya. Prof D N Rao from AIIMS, New Delhi, constructed Multiple Antigenic Peptide (MAP) based on in house established immunodominant B and T cell epitopes of E2 protein and established an alternative approach for vaccine design for Chikungunya. With the aim to identify immunodominant epitopes within the envelope protein his team investigated the detailed analysis of fine specificity of antibody response in different individuals with Chikungunya Virus infection.

Autoimmunity is an aberrant immune response against the self-tolerance mechanism. Because of its intricate pathogenesis, therapeutics is still evolving. The incidence of autoimmune colitis has been progressively increasing globally. Human lymphatic filariae have evolved numerous immune evasion strategies to secure their long-term survival in a host. Prof Kalyan Goswami from AIIMS, Kalyani showed that exploiting filarial immunomodulators can be a potential therapeutic strategy against autoimmune pathology. Dr. Vijay Kumar Kutala from Nizam's Institute of Medical Sciences (NIMS), Hyderabad, investigated the association of human leukocyte antigenclass II alleles with the susceptibility and phenotypic heterogeneity of systemic lupus erythematosus (SLE) in south Indian subjects.

Dr. Sukhes Mukherjee from AIIMS, Bhopal revealed that *M olifera* phytocompounds have potent anti-breastcancer properties in cell lines, suggesting that Tregs and peripheral immune cell counts could be used as biomarkers for breast cancer diagnosis and prognosis. Injamam Ul Hossain from JIPMER, Puducherry, compared the serum levels of oncovascular risk factors, stress levels and vascular endothelial function before and after Neoadjuvant Chemotherapy (NACT) among primary Breast Cancer (BC) patients.

Apart from scientific deliberation all delegates enjoyed nature walk along dam on Muraddi Lake and lush green and dense forest of blooming flame of the forest, Palash.

Delegates also witnessed famous Chhau (also spelled Chhou), a semi classical Indian dance with martial and folk traditions of Purulia. The program was jointly supported by Association of Clinical Biochemists of India (ACBI), Indian Immunology Society (IIS), Indian Immunology Foundation (IIF). This memorable program at Baranti Village Resort ended with Vote of thanks by the Organizing Secretary Dr Mrityunjoy Halder.

National Society Report- CACB Taiwan

NAME OF SOCIETY	Chinese Association for Clinical Biochemistry (CACB-Taiwan)
OFFICIAL SOCIETY EMAIL ADDRESS	office@cacb.org.tw
NAME OF PRESIDENT & EMAIL ADDRESS	Sandy Huey-Jen Hsu sandyhsu@ntu.edu.tw
NAME OF NATIONAL REPRESENTATIVE TO APFCB & EMAIL ADDRESS	Woei-horng Fang whfang@ntu.edu.tw

REPORT ON SOCIETY ACTIVITIES

CACB annual conference and scientific symposium were held in conjunction with the 38th Joint Annual Conference of Biomedical Science (JACBS) on March 23rd and 24th, 2024. The main theme for JACBS 2024 was “Biomedicine and Life”. Dr. Man-Ho Choi, Principal Scientist at Korea Institute of Science and Technology, delivered a keynote speech regarding steroidogenesis in adrenal diseases. Three speakers, Dr. Cheng-Hsun Chiu, Dr. Wei-Kai Wu and Professor Hsin-Chih Lai were invited to share their expertise of “microbiome in health and disease”. Dr. Chiu shared updates on gut microbiome and microbiome-based therapeutics. Dr. Wu focused on quantification of fecal bbu Genes predicts L-carnitine-mediated TMAO production. Dr. Lai emphasized on the current development of the next generation probiotics. Following the symposium, student’s research oral presentation competition and poster contest were also held. Overall, the two- day conference was very stimulating and truly a delightful academic gathering for the attending members of CACB.

(Photo 1) Keynote speaker Dr. Man-Ho Choi at the 38th JACBS.

(Photo 2) CACB board members at the 38th JACBS.

(Photo 3) Winners of the poster contest and CACB president, Dr. Sandy Huey-Jen Hsu (center).

Upcoming events for 2024:

CACB will hold a special workshop on “patient-based quality control”, featuring the esteemed APFCB traveling lecturer, Dr. Tze Ping Loh. This event will be held on October 12th, 2024 at National Taiwan University Hospital and promises to be an enriching experience for all participants including CACB members and students in the field of Clinical Laboratory Sciences.

National Society Report – NACC Nepal

Nepalese Association for Clinical Chemistry (NACC)

Prepared by: Dr. Ram Vinod Mahato, Secretary General, NACC- Nepal

Name of Society	Nepalese Association for Clinical Chemistry Email: nacc2070@gmail.com
Name of President	Prof. Dr. Madhab Lamsal (madhab.lamsal@bpkihs.edu)
Name of National Representative General Secretary	Dr. Ram Vinod Mahato (ramvinodmahato42@gmail.com)
Senior Vice President	Prof. Dr. Prabodh Risal
Vice President	Dr. Vijay Kumar Sharma
Treasurer	Dr. Santosh Pradhan
Secretary	Mr. Raju Kumar Dubey

REPORT ON SOCIETY ACTIVITIES

The Nepalese Association for Clinical Chemistry (NACC) is a National scientific and professional organization representing clinical Biochemists across Nepal. NACC is member society of International Federation for Clinical Chemistry and Laboratory Medicine (IFCC) and Asia Pacific Federation for Clinical Biochemistry (APFCB) working in the field of clinical chemistry and laboratory medicine. It was established on 25th February 2014 with more than 150 professionals (MD/MSc/DM/PhD) and postgraduate students in Biochemistry working in the field of Clinical Chemistry and Laboratory Medicine, health care set-ups, academics and research. NACCON2024 and 4thAnnual General Meeting with scientific symposium held at the Kist Medical College and Teaching Hospital, Lalitpur on April 27 2024. The theme was “Current & Emerging Trends in Clinical Chemistry”. Two speakers were invited to present the progress on Emerging Trends in Clinical Chemistry and its applications. International speaker Prof. Dr. Kun-Young Sohn, Cinical Biochemist, Laboratory Medicine and Genetics Program at Trillium Health partner, Canada delivered speech on the Topic: "Intra-Operative Monitoring of PTH/Adrenal Venous Sampling for Primary Aldosteronism". Speaker from Nepal Associate Prof. Dr. BijayaMishra from BP Koirala Institute of Health Science, Dharandelivered speech on topic: "Newborn Screening Early detection Matters".Overall, the one-day symposium was very successful and truly an enjoyable academic gathering for more than 150 attendees.

Upcoming events for 2025: NACChas scheduled to organize a workshop with ADLM in April, 2025

(Photo 1) Members of NACC Executive committee formed during the Annual General Meeting 2024.

(Photo 2) Participants during the annual general meeting 2024.

(Photo 3) Presenting Token of Appreciation to Prof. Dr. Kun-Young Sohn

(Photo 4) Presenting certificate of Appreciation to Assoc. Prof. Dr. Bijaya Mishra

(Photo 5) Special Guests during the Symposium 2024

(Photo 6) Photo with SNIBE (Sponsor)

Photo 1: Prof. Dr. MadhabLamsal, Prof. Dr. PrabodhRisal, Dr. Vijay kumarSharma, Dr. Ram VinodMahato, Dr. Santosh Pradhan, Mr. RajukumarDubey, Dr. AsmitaPokhrel, Dr. BijayaMishra, Dr. Binod kumarYadav, Dr. BishalRaj Joshi, Dr. RanjanSuwal, Dr. SarojThapa, Dr. ShravankumarMishra, Mr. BasantaGelal, Mr. ManojSigdel, Mr. RakeshPokharel, Mr. Shantossubedee, Mr. Sumansapkota, Mr. Tapeshwaryadav

Photo 2: NACC members participating in annual general Meting

Photo 3: Presenting token of appreciation to guest speaker Prof. KUN Young SOHN

Photo 4: Prof. MadhavGautam presenting certificate of appreciation to guest speaker Dr. Bijaya

Photo 5: Special Guests during the Symposium

Photo 6: Photo SNIBE (Sponsor)

IFCC World Lab 2024 – Dubai: Special Opportunities for Young Scientists

Prepared by: Tara Rolić, Croatian YS, Josep Miquel Bauçà, Spanish YS, and Kamil Taha Uçar Turkish YS

The 26th WorldLab - IFCC International Congress in Clinical Chemistry and Laboratory Medicine was held in Dubai (UAE) from May 26th to 30th, 2024. During the congress, Young Scientists (YS) had opportunities to participate in dedicated activities. YS were encouraged to share their high-quality scientific work, to network, and to continue to build their careers as laboratory professionals and future leaders.

3rd Young Scientist Forum

The 3rd Young Scientist Forum provided attendees, speakers, moderators, and organizers with a fantastic opportunity to present their specific and professional work and connect with young colleagues from around the world facing similar challenges and sharing the same enthusiasm for their profession. Held just before the opening of the 26th International Congress of Clinical Chemistry and Laboratory Medicine, the forum saw over 200 registered young scientists. The three sessions of the day focused on 1) digital technology innovations in laboratory medicine, 2) clinical case reports, 3) Future of Laboratory Medicine and YS leadership. Thanks to the remarkable support of the IFCC and notable figures such as Prof. Tomris Ozben, Prof. Khosrow Adeli, Dr. Maryam Matar, Dr. Eduardo Freggiaro, Dr. Alvaro Justiniano, and Prof. Rajiv Erasmus, the forum provided a fruitful scientific, professional, and personal networking experience.

1st young scientist's poster session at WorldLab 2024 in Dubaï (Report by Marie Lenski, French YS and Claudia IMPERIALI, Spanish YS, both members of the IFCC-TF-YS)

The IFCC Task Force - Young Scientists (IFCC TF-YS) organized the 1st « Young Scientist poster tour ». Young professionals had 5 minutes to present and 5 minutes to answer questions to defend their work in front of a jury made up of two members: one IFCC officer and one member of the IFCC TF-YS. A total of 60 young scientists participated to this activity, along with 20 jury members. All participants received a certificate of participation, and ten young scientists were selected for the Best Poster Presentation award. The IFCC TF-YS would like to thank the IFCC officers who participated or offered their participation in this activity.

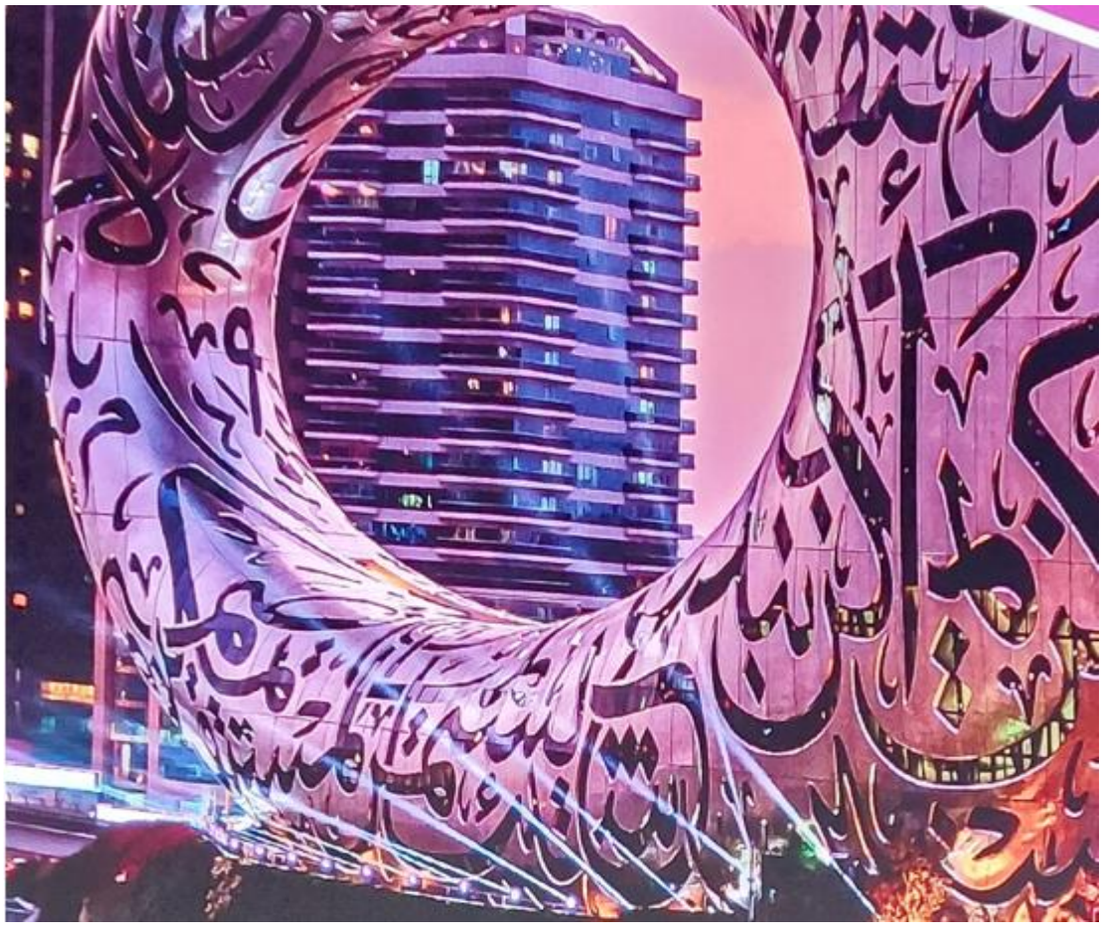
YS excursion to the University City of Sharjah (Report by Judit GONDA, Hungarian YS)

Young Scientists had an opportunity to make a full-day visit on 29 May to the University City of Sharjah. Sharjah is the northern neighbouring emirate of Dubai and the third-most populous city in the United Arab Emirates. Firstly, we were taken to Sharjah Research Technology and Innovation Park (SRTIP). The Park is focused on promoting research, technology, and innovation in various fields, including healthcare, energy, environment, and technology. Our second program was a guided bus tour through the whole University City. Our next program was a visit to the University of Sharjah Medical Campus Research Institute for Medical and Health Sciences (RIMHS). The RIMHS excels in its new research environment, with its schools of biomedical/biotechnology sciences, dental medicine, medicine, and pharmacy. Lastly, we visited the Holy Quran Academy. The Academy includes several museums, offer scientific courses, and has a specialised library. We returned to Dubai at the end of the day with

broadened scientific horizons and cultural experience. Many thanks to Dr Shaikha Almazrouei for organising our trip and to Fady AbdulNasser AbuKhadra for coordinating our group throughout the whole day!

YS award (Report by Marie Lenski, French YS and member of the IFCC-TF-YS)
This year, one Young Scientist, Dr David Bartélémy, has been selected to receive the 2024 IFCC-Gérard Siest Young Scientist Award for Distinguished Contributions in Pharmacogenetics, sponsored by Biologie Prospective. Dr David Bartélémy is a young specialist in laboratory medicine (PharmD, PhD) who joined the Biochemistry and Molecular Biology Department of the Hospices Civils de Lyon, France, in 2018. His research activities in pharmacogenetics aim to improve sequencing technologies and evaluate the variability of pharmacogenetic profiles for complex pharmacogenes such as CYP2D6, UGT1A1, and NAT2. This award recognizes his contribution to advancing the scientific discipline of pharmacogenomics and Personalized/Precision Medicine.

The next EFLM-IFCC congress 2025 will be in Brussels, Belgium. The IFCC TF-YS is already involved in the preparation of young scientists dedicated activities, in collaboration with the EFLM Task-Group Young Scientists (EFLM TG-YS) and groups of YS from national federations of specialists in laboratory medicine, to facilitate new opportunities for young scientists.



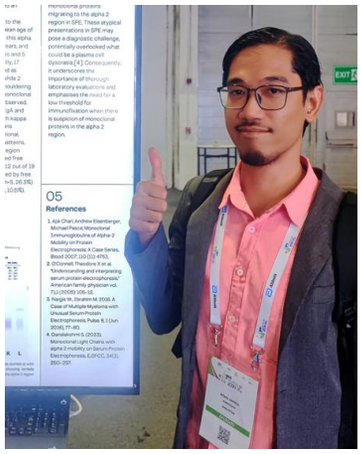
IFCC WorldLab 2024: Dubai through Young Scientists' Eyes, Asia-Pacific Edition

Prepared by: Udara Senarathne, Sri Lanka - Task Force for Young Scientists

The IFCC WorldLab 2024 - International Congress in Clinical Chemistry and Laboratory Medicine was held in Dubai (UAE) from 26-30 May 2024, with the 3rd edition of the Young Scientists' Forum held on 26th of May, 2024 at the Conrad Hotel. The YS forum was attended by over 200 young scientists and had three sessions including digital technology innovations in laboratory medicine, clinical case reports, the future of laboratory medicine, and YS leadership. During the congress, young scientists had the chance to engage in many activities, including the first YS Poster session and they were encouraged to present their scientific research, network with peers, and further their careers as laboratory professionals and future leaders. The forum, made possible by the exceptional support of the IFCC leaders including Prof. Tomris Ozben, Prof. Khosrow Adeli, Dr. Maryam Matar, Dr. Eduardo Freggiaro, Dr. Alvaro Justiniano, and Prof. Rajiv Erasmus, offered a valuable experience for scientific, professional, and personal networking. This article summarises the comments from young scientists from the Asia-Pacific region who participated in the 26th IFCC WorldLab-Dubai.

Zeenath Thaneefa
North Colombo Teaching Hospital – Sri Lanka

In the IFCC World Lab 2024, I had an enriching experience exploring the latest advancements in clinical chemistry and laboratory medicine. The diverse range of presentations and workshops provided valuable insights into cutting-edge research and technology. Networking with professionals from around the globe further enhanced my understanding and passion for this dynamic field, leaving me inspired and motivated to contribute more effectively to healthcare through laboratory sciences.



Mohd Amirul

Hospital Ampang – Malaysia

Attending the IFCC Congress in Dubai was a truly remarkable and enriching experience, which was made possible by the generous IFCC Travel Grant Scholarship. As a young Chemical Pathology trainee this was my first international scientific congress, and the atmosphere was exhilarating. One of the highlights was the opportunity to present my research during the elevator pitch session. The chance to share my work and receive feedback from experts in the field was an unparalleled learning opportunity. The congress itself was a treasure of knowledge, covering a wide range of topics in laboratory medicine.

Sudhahar Tamizhan

Dept of Biochemistry, AIIMS Rishikesh – India

Vanakkam! Namasthe! It was One of the best International Conferences! At the IFCC YS Forum, I was particularly impressed by the depth of discussions around emerging technologies and their potential to revolutionize patient care. The passion and creativity displayed by the young scientists were palpable, creating an environment ripe for networking and the cultivation of future leaders in the field. The keynote presentations were not only informative but also motivational, emphasizing the critical role that innovation and interdisciplinary collaboration play in advancing healthcare. I was part of the Young Scientists Forum which opened my eyes to Innovation, Extraordinary development, and Applications.

Pavithra Samarakoon
Sri Lanka

As a medical professional working in a laboratory setup and making physicians understand the importance of laboratory medicine as a part of patient care, it was an important opportunity to see and experience the advancement of laboratory medicine at the international level. Also to learn how this could be applied in our local setup for patients' benefit. And it was great to feel "belonged" in a world of laboratory sciences and young scientists with the same enthusiasm.

Sathya Selvarajan
MGM HEALTHCARE CHENNAI, Tamil Nadu – India

The Young Scientists Forum at IFCC WorldLab Congress Dubai 2024 provided an excellent platform to network with peers globally and exchange ideas on research and subject matters. I actively participated in dynamic networking sessions and presented my research at the Poster Tour, where I was honored to receive an award for the best poster. I am truly grateful for the encouragement, recognition, and suggestions provided by the forum. This experience highlighted the importance of emerging trends and leadership skills in clinical biochemistry, and the insights and connections I gained will significantly influence my future work and career development.

Rupali Bains

Dept of Biochemistry, AIIMS Rishikesh – India

My best experience at the IFCC YS Forum on May 26th was witnessing the dynamic exchange of innovative ideas among young scientists, fostering a sense of collaboration and inspiration. The forum's vibrant atmosphere highlighted the potential for groundbreaking advancements in clinical chemistry and laboratory medicine.

Rajan Paudel

Nepal Association for Medical Laboratory Sciences (NAMLS) – Nepal

Having been awarded the IFCC Travel Scholarship, I was able to participate in the Third IFCC Forum for Young Scientists as well as IFCC WorldLab 2024 - Dubai, UAE. I had the honor of presenting my research findings at the IFCC WorldLab 2024 Young Scientists Poster Tour. I was motivated to seek out more expertise in our profession by this platform. In addition, the occasion offered me a fantastic chance to network with both seasoned professionals and aspiring scientists, as well as to gain valuable insights and feedback. These interactions have broadened my view of the world via the lens of laboratory medicine. I would like to express my sincere gratitude to the IFCC for providing me with the "IFCC Travel Scholarship" so that I could attend the XXVI International Congress of Clinical Chemistry and Laboratory Medicine and the IFCC Forum for Young Scientists in Dubai (UAE) from May 26 to 30, 2024, and for making such a worthwhile and educational event. This event has been a major turning point in my laboratory medicine career and future aspirations.

Menaka Balasooriya
Sri Lanka

Participating in the IFCC YS Forum was instrumental in updating and expanding my knowledge of laboratory medicine, providing me with a comprehensive understanding of current trends and challenges in the field. Additionally, I had the opportunity to present my research and receive valuable constructive feedback. This experience was a remarkable platform to share my work from Sr Lanka with researchers worldwide. The connections I made with researchers who share similar interests will foster future collaborations, explore new avenues, and potentially inspire innovative projects aimed at enhancing lab testing.

Kim G. Sarong
Silliman University – Philippines

Attending the IFCC Young Scientists Forum on May 26th, 2024, at the Conrad Hotel in Dubai was a remarkable experience, highlighted by the insightful presentations and dynamic discussions on cutting-edge advancements in clinical chemistry. The networking opportunities with fellow young scientists from around the world were invaluable, fostering collaboration and inspiring future innovations in the field.

Ratna Apriyanti

Prodia Clinical Laboratory – Indonesia

It was a very valuable experience for me to have the opportunity to attend the 3rd Young Scientist Forum IFCC which was held on 26 May 2024 in Dubai. YS Forum has become a forum for exchanging ideas and learning about new research that can provide mutual insight into the scope of research and work of fellow scientists in various countries and learn about leadership and laboratory management which is very useful. Of course, we will have a wider network around the world of scientists. I would like to thank all the committee members who made this forum a success.

Marina Shah

Universiti Malaya and Hospital Kuala Lumpur – Malaysia

As an introvert, I initially felt overwhelmed by the enthusiastic crowd at the Young Scientists Forum. However, the forum provided a great platform for networking, sharing ideas, and learning from peers. Witnessing the passion of these young researchers in improving their respective healthcare sectors inspired me greatly. I am very glad to have been given the opportunity to be there. Looking forward to future activities by YS-TF.

Hira Azeem

Aga Khan University Hospital, Karachi – Pakistan

I am deeply honoured to have attended the IFCC Forum on May 26th. Attending the IFCC Young Scientists Forum was a transformative experience that allowed me to network with peers and learn from leading experts in the field. It was truly an inspiring event. This esteemed event offered young scientists from around the world a platform to show case their research, exchange experiences, build connections, and explore potential collaborations. I extend my heartfelt gratitude to all the organizers for orchestrating such a successful forum, with special thanks to Dr. Santiago and Dr. Shaikha.

Dipesh Tamrakar

Nepal Association for Medical Laboratory Sciences (NAMLS) – Nepal

The IFCC YS Forum on May 26, 2024, was my very first experience attending a live session of an international conference. There was an electrifying and inspiring atmosphere of passionate young scientists from diverse backgrounds who shared groundbreaking ideas, fostering collaboration and innovation that promised to shape the future of laboratory medicine. I am delighted by the event and excited to attend more such events soon.

Janani Ramesh

ESIC Medical College and Hospital, Chennai-India

Attending the IFCC WorldLab 2024 was a truly unforgettable experience. It provided a platform to learn about the current advances in the field of Clinical Chemistry. The 3rd IFCC Young Scientists Forum on May 26th was particularly enriching. Collaborating and networking with young scientists from across the globe was inspiring. The “mentor-mentee “session during the forum gave us the opportunity to brainstorm various ideas regarding lab management and other issues faced by a budding laboratory physician. I also had the opportunity to interact with distinguished faculties from various parts of the world. Looking forward to taking part in more YS-TF activities.

Lisa Tamang Ghising

B.P. Koirala Institute of Health Sciences – Nepal

As a recent MD Biochemistry graduate, I was immensely elated to participate in the magnificent IFCC Forum for Young Scientists. The forum offered an excellent opportunity to exchange ideas with brilliant young minds and meet exceptionally talented mentors and laboratory medicine professionals from all around the globe. I learned about different cutting-edge research, and innovations in the field and was delighted to witness the active collaboration and integration of laboratory medicine by the enthusiastic Young Scientists Task Force. I express my profound gratitude to the IFCC for granting me with Travel Scholarship and enabling my debut at an international conference, for my professional development.

Juliyatin Putri Utami
University of Lambung Mangkurat – Indonesia

Young Scientist Forum in Dubai was my second event. I found that every year YS-TF always brought up to date, rich and delightful issue about laboratory medicine to all young scientists. I am glad to be part of this event.

Young Scientist Interview

Full Name: Xincen "Luke" Duan
Affiliation: Zhongshan Hospital, Fudan University
Address: 180 Fenglin Road Xuhui, Shanghai, China
Professional society's affiliation: Chinese Society of Laboratory Medicine

Please introduce yourself?

I'm Xincen Duan, but you can call me Luke. I was born and raised in Kunming, a southwest city in China known as the "Spring City" because of its great weather. A blend of international and interdisciplinary experiences has marked my academic pursuits. After high school, I pursued higher studies in the United States, obtaining a Bachelor's degree in Biological Science with a focus on Pre-Health and also minored in business management from the University of Wisconsin, Parkside. Later, I finished my Master of Predictive Analytics (now Data Science) at DePaul University in Chicago, which laid the foundation for my expertise in data science. In 2018, I returned to Shanghai, joining Zhongshan Hospital, Fudan University, as a data scientist. At the same time, I completed my PhD in Laboratory Medicine, reflecting my dedication to both research and clinical applications. Currently, I serve as a dedicated researcher and data scientist at Zhongshan Hospital, where I apply my analytical skills to enhance medical diagnostics and patient care.

What is your main focus?

I've been working on several projects that use data-driven approaches to solve problems in clinical laboratories. Among all of the projects, my main focus right now is on improving the theories behind patient-based real-time quality control (PBRTQC) and supervising software development. The project has been ongoing for over five years. We made a breakthrough in 2021 with our publication in Clinical Chemistry, which demonstrated the regression-adjusted real-time quality control framework that significantly improved the performance of PBRTQC models. Recently, my team and I have been working on developing an intelligent and user-friendly software system to assist laboratories in leveraging the potential of PBRTQC to improve quality assurance at a manageable cost. The software is now in beta, with approximately five tertiary hospitals on trial. We plan to launch an international online version of the software before the 2024 APFCB congress, allowing our international audience to benefit from the new technology.

What else is important to you?

Aside from efforts to improve PBRTQC, I've been working on a number of projects to increase work efficiency in clinical laboratories. We created a multimodality machine learning model to enhance the interpretability of immunofixation electrophoresis. The multimodal algorithm can interpret both the immunofixation plot and the serum protein electrophoresis results simultaneously. The information in serum protein electrophoresis can help the machine learning model perform better.

We also worked on improving phlebotomy tube utilization by using a variant of the classic text-mining method, the term frequency-inverse document frequency (TF-IDF), to identify the relationship between the existing rules for combining different tests in a single phlebotomy tube.
The findings help our laboratory optimize our combination rules and save approximately 2% of total phlebotomy tube usage.

What are your interests in biomedical lab medicine?

The previous questions probably do a good job showing where my interests lie in biomedical lab medicine. However, from a more general perspective, my interests focus on mining the value within the data in clinical laboratories. I hope the insight and value generated from our work can benefit workflow efficiency in clinical laboratories and the service to physicians and patients.

What are your future goals?

Building a "smart" clinical laboratory represents one of the most exhilarating frontiers in laboratory medicine today. I am both excited and challenged by the vast opportunities this field presents. My future goals are directed toward overcoming significant challenges and pushing the boundaries of what's possible. Firstly, I want to improve education and training programs to equip clinical laboratorians with advanced knowledge in data science and information technology. This will empower them to harness the full potential of data in their work. Secondly, I want to address data management's ethical, security, and standardization aspects. I hope to develop protocols that ensure a robust, secure, and ethical environment for data analysis, safeguarding patient privacy while fostering trust. Also, I want to work on standards that improve interoperability and standardization across the information system across various institutions. By establishing standard data formats and exchange protocols, we can break down silos and facilitate a more integrated approach to patient care. By focusing on these objectives, I aspire to play a pivotal role in shaping the future of clinical laboratories, where intelligence, efficiency, and empathy converge to deliver the best possible care to patients.

Interviewer

Dr. Vivek Pant

Consultant Biochemist and Head- Research Unit, Samyak Diagnostic Pvt Ltd, Kathmandu, Nepal.
Corresponding member, Task Force Young Scientist, IFCC.
Corresponding member, Task Force on Outcome Studies in Laboratory Medicine, IFCC.
Corresponding member, Communication and Publication division, APFCB.

Meeting an Expert

Full Name: Professor Dr. Mohd Nazil Salleh

Affiliation: Faculty of Health Sciences, University College of MAIWP International, Taman Batu Muda, Batu Caves 68100 Wilayah Persekutuan, Kuala Lumpur, Malaysia
Address: University College of MAIWP International, Taman Batu Muda, Batu Caves 68100 Wilayah Persekutuan, Kuala Lumpur, Malaysia
Professional society's affiliation: Deputy Vice-Chancellor, Academic, Research and Internationalization, University College of MAIWP International, Kuala Lumpur Malaysia
Chartered Scientist, Institute of Biomedical Science, United Kingdom
President, Malaysia Confederation of Allied Health Professional Association, Malaysia
President-Elect, ASEAN Association of Schools Medical Technology
President-Elect, Malaysia Institute of Medical Laboratory Malaysia
Visiting Professor in Biomedical Science, Universities Qamarul Huda Badaruddin Bagu, Mataram, Indonesia

Please introduce yourself?

I'm Dr. Mohd Nazil Salleh, CSci, Ph.D., a distinguished professor in Biomedical Sciences. I hold a PhD in Molecular Genetics, a Master's degree from the University Putra Malaysia, and a BSc. in Biomedical Science from Bradford University, UK. From 2019 until now, I have occupied the esteemed position of Deputy Vice-Chancellor of Academic, Research and Internationalisation at the University College of MAIWP International, Kuala Lumpur, Malaysia. In 2019, I was appointed as an Adjunct Professor in Medical Technologist from the Mataram Polytechnic College, Lombok, West Nusa Tenggara, Indonesia, to contribute to the development of the academic program for the Polytechnic. In 2024, I was appointed as a visiting Professor from Universitas Qamarul Huda Badaruddin, Praya Central Lombok, West Nusa Tenggara, Indonesia, to strengthen the Master's program in Public Health. My remarkable achievements in Biomedical Science have garnered significant recognition, being the first Malaysian to be accredited as a Chartered Scientist by the Science Council, UK, and a fellow member of the Institute of Biomedical Science (IBMS) and Society of Biology (SB), United Kingdom in 2014 and 2015 respectively. I have been honoured with numerous prestigious awards, including scientific recognition through the Wellcome Trust Sanger Institute Fellowship in 2014 and the European Molecular Biology Organization (EMBO) Fellowship. As a prominent leader in Biomedical Science, I also received the Malaysia Outstanding Personality Award in the Biomedical Sciences category from Malaysia Education TVET Awards 2022, organised by the Ministry of Education Malaysia, and the Highest Recognition (Anugerah Tertinggi) during the 10th Convocation of Polytechnic College, Lombok, West Nusa Tenggara, Indonesia in 2022

What is your main focus?

For over 16 years, I have been an integral part of Malaysia Qualifying Agency (MQA) accreditation teams as a panel and chairman assessor for Biomedical Sciences programs at the undergraduate and postgraduate levels. I have held various academic and administrative positions and faculty roles for over 20 years, accumulating 27 years of teaching experience in Biomedical Science programs at the undergraduate and postgraduate levels. My extensive 30 years of experience training researchers in general Biomedical Sciences and molecular biological techniques as research tools have been invaluable to the field. Besides teaching undergraduates, I also supervised postgraduates at the MSc and PhD national and international levels. As the Editor-in-Chief of the Malaysian Journal of Medical Laboratory Sciences, I have authored and co-authored 40 scientific papers published and presented in national and international journals, seminars, workshops, symposiums, and conferences.

What else is important to you?

I had a passion for constructing various objects, including using LEGO, and I found joy in mathematics; my proficiency in it was always exceptional. Regardless of the scientific field you pursue, mathematics will always be an indispensable component, and practical communication skills are equally essential. While the 20th century witnessed numerous groundbreaking discoveries in biomedical sciences, transforming our daily routines by introducing numerous technologies, I am confident that the current century will witness significant progress in healthcare and the fundamental comprehension of cellular structures. Anticipate advancements in human longevity, treating previously incurable illnesses, and emerging innovative technologies that will shape our future.

What are your interests in biomedical laboratory medicine?

My active involvement in Biomedical Science is evident through my contributions as part of a task force of the Allied Health Professions Act 2016 (Act 774), appointed by Malaysian Allied Health Professions, Ministry of Health, Malaysia, between 2016 and 2019. In 2023, I was appointed to a joint technical committee for the Allied Health Professions Council to represent private higher institutions, especially in endorsing new and verified academic programs under the allied health profession. I have also served as a fellow and executive council member of the Malaysia Institute of Medical Laboratory Science since 2014. In 2024, I was elected president of the Malaysia Confederation of Allied Health Professional Association (MyCAHP) for the next two (2) years. On an international level, Prof. Dr Mohd Nazil has been an esteemed Executive Council member since 2016 and was elected as the Vice President of the ASEAN Association of Schools Medical Technology (AASMT) in 2021, representing Malaysia and bringing pride to the nation. During the COVID-19 pandemic in 2020, the International Federation of Biomedical Laboratory Science (IFBLS) acknowledged my expertise in Molecular Biology to assist in reviewing WHO documents. In addition, during the era and post-COVID-19, he actively contributed as an invited speaker on the virtual platform in molecular diagnostics set-up and knowledge sharing in the biomedical sciences area.

What are your future goals?

My unique demeanour, a blend of humility and authority in my speech, reflects my profound knowledge of Biomedical Sciences. This distinctive quality sets me apart as a remarkable role model in the field of research, inspiring many.

Interviewer

Dr. Ryunosuke OHKAWA

Professor, Department of Clinical Bioanalysis and Molecular Biology, Graduate School of Medical and Dental Sciences (TMDU), Japan.

Board member, JCLS (Japan Association for Clinical Laboratory Science),

Board member, JSCC (Japanese Society of Clinical Chemistry)

Board member, JCCLS (Japanese Committee for Clinical Laboratory Standards)

Councilor, JSLM (Japanese of Society of Laboratory Medicine)

Councilor, JAMT (Japanese Association of Medical Technology Education)

Previous corresponding member of Task Force Young Scientists, IFCC (International Federation of Clinical Chemistry and Laboratory Medicine) Member, Communication and Publication division, APFCB

Roche Diagnostics Asia Pacific

Event Summary for APAC-IRIDS (International Roche Infectious Diseases Symposium)

The inaugural International Roche Infectious Diseases Symposium (IRIDS) in Asia Pacific marked an exciting and groundbreaking milestone for Roche Diagnostics Asia Pacific , where we solidified our commitment to being a partner for the community in the infectious diseases space. Spanning across one and a half days, from 19 to 20 June in Ho Chi Minh City, Vietnam APAC-IRIDS 2024 brought together laboratory experts, clinical specialists and policy makers from across the APAC region and globally.

The theme was **"Looking Back, Leaping Forward",** which aimed to reflect on the past, evaluate current practices, envision the infectious disease landscape of tomorrow, while charting the path for the future. Together with our partners throughout the ecosystem, we work to address common challenges and find solutions.

Event Highlights

Together there were a total of 248 participants. APAC-IRIDS served as a bridge, helping experts network and creating opportunities for KOLs from different countries to engage in in-depth discussions on various policy implementations.

A customer satisfaction score (CSAT) score of 93.4% and net promoter score (NPS) of 59.3 was given to the event.

Agenda Highlights

APAC-IRIDS featured diverse perspectives on infectious disease from local, regional, and global KOLs, including Dr. John Ward, Coalition for Global Hepatitis Elimination. They discussed diseases such as hepatitis, respiratory diseases including tuberculosis, transplant, and antimicrobial resistance. Additional topics including real world evidence, AI based screening, predictive algorithms were also discussed including their applications in various settings.

One of the newer initiatives in the agenda was the addition of a fireside chat-styled panel session that had speakers from the APAC Liver Diseases Alliance come together to discuss how hepatitis elimination could be achieved. Moderated by Dr Roberta Sarno, Director of the APAC Liver Disease Alliance, the stage was shared by Dr John Ward, Coalition for Global Hepatitis Elimination, Dr Vu Ngoc Bao, Senior Technical Director HIV/TB/Hepatitis, PATH Vietnam, as well as Ms Yuhui Chan from the Clinton Health Access Initiative.

Aligning with the meeting's theme, the topics encouraged participants to consider both current challenges and future innovations for disease elimination.

The journey to becoming a partner in infectious diseases is ongoing. APAC-IRIDS has been pivotal in this, enhancing infectious diseases understanding and testing advocacy across APAC.

The 'Great Trans-Atlantic Acid-Base Debate: Current Status in the age of Artificial Intelligence

Corresponding Author:

Prof Aamir Ijaz
MBBS, FCPS, FRCP(Edin), MCPS-HPE
Prof of Chemical Pathology
NUST School of Health Sciences Islamabad, PAKISTAN
Ex-President Pakistan Society of Chemical Pathologists (PSCP)
Country Rep APFCB
Member Education Committee APFCB
email: aamirijaz@nshs.nust.edu.pk

Abstract

Blood gas analysis (BGA) is one of the most common investigations carried out in critically ill patients. All the results mentioned in the print-out from the BGA equipment are not measured directly but some are calculated using formulae devised by great scientists like Henderson and Hasselbalch. Similarly, in 1950s, interpretation rules were suggested by a group of scientists from Boston Massachusetts US. These rules were based on two BGA parameters i.e. partial pressure of arterial Carbon Dioxide ($PaCO_2$) and concentration of bicarbonate [HCO_3].These rules were, however, criticized on the plea that some 'extra luggage' has been added on a cognitively over-loaded plethora of symbols appearing 'Latin' to a novice. In Copenhagen (Denmark), on other side of the Atlantic Ocean, some parameters were proposed for quantitative assessment of metabolic acid-base abnormalities. These include Standard Bicarbonate ($stHCO_3$), Base Excess (BE) and Standard Base (SBE). These parameters were severely criticized by Boston Group mainly on the ground that these parameters are derived 'in vitro' and not valid for 'in vivo'. Such debates are quite desirable and must continue by the new generations of scientists to find a solution based on Artificial Intelligence, so that the machines should not only give the data (plethora of symbols) but also exact diagnosis of acid-base disorders, stoichiometric analysis and the amount of acid or base required to be given to the patient.

Keywords:

Metabolic Acidosis; Base Excess; Standard Bicarbonate; Standard Base Excess, The Great Trans-Atlantic Debate revolves around two schools of thought about the interpretation of Blood Gas Analysis (BGA) reports. The controversy in the words of Dr TJ Morgan is "at a given PaCO2 and pH, what is the best tool to delineate the separate respiratory and metabolic contributions to the overall acid-base status?"
(1) Let us examine this debate in some details:

Historical Perspective

As students of Clinical Biochemistry, we should be familiar with (as a neutral observer) this controversy spanning now over more than six decades and it continues in 2024, too.

The Parties Across the Atlantic

a. **Boston:** Schwartz, Relman and colleagues at Tufts University Boston Massachusetts US (Western side of Atlantic Ocean)

b**. Copenhagen:** K Jorgensen, Poul Astrup, Ole Siggaard-Andersen, N Fogh-Andersen (Eastern side of Atlantic Ocean). But this school of thought has big names to support from outside Denmark too, e.g. TJ Morgan (Australia) (his book chapter provided me the framework for this article) and JW Severinghaus (USA) (The inventor of CO_2 Electrode and BGA equipment). So, this debate is not limited to the Geographical boundaries.

c. **Canada:** Peter Stewart's 'Strong Ion Difference' - semi-quantitative analysis using principles of physical chemistry was a major conceptual shift. We worked on this system and found no additional advantage over traditional system, so for the sake of brevity, we will not include this school of thought in the present article (2) .

The Points of Agreement

Like a good arbitrator we must first bring forward the points agreed between the two parties:

a. Acidaemia as arterial pH<7.35,
b. Alkalaemia as pH>7.45.
c. Respiratory acidosis is when $PaCO_2$ > 45 mmHg
d. Respiratory alkalosis is $PaCO_2$ is < 35 mmHg.
e. Metabolic (non-respiratory) acid-base abnormalities manifest on blood gas analysis as a disturbed pH/ $PaCO_2$ relationship(1)

What exactly is the Controversy?

Background: when BGA report comes to a Chemical Pathologist or a Clinician, the primary disorders and compensatory changes are not marked on it, meaning the interpreter must delineate the metabolic and respiratory pathologies herself or himself.

The Difference: The debate is to select the best tool to find the compensatory change and whether the compensatory change is physiologic, or it is a double or triple ABD. Furthermore, the quantitative analysis of how much acidosis or alkalosis is present.

Rule of the Game

Let us first set the rule of the game i.e. the criteria of a good tool to find the compensatory change. Since we will use it on the bedside of patient, the ideal index for metabolic acid-base analysis should have following characteristics:

a. Simple and "user friendly"
b. Independent of $PaCO_2$ (CO_2-invariant).
c. Stoichiometric: This means that the index should be able to quantify the amount of strong acid or base (expressed as mmol/L extracellular fluid) which would correct any metabolic acid-base disturbance (3)

The Contending Parameters:

a. The $PaCO_2$/ $[HCO_3^-]$ based "rules" of the Boston school.
b. Standard base excess of Copenhagen school.

The Boston "Rules"

a. Six equations were developed by Schwartz, Relman and colleagues at Tufts University and are the foundation of Boston School (4)
b. The six equations examine either the $[HCO_3]$ in primary respiratory disturbances or the $PaCO_2$ in primary metabolic disturbances. (1).
c. These rules are widely used in medical set-ups. (5),(6),(7)
d. We have developed 'One Minute Decoder' based on Boston Rules for the interpretation of BGA reports by a novice (junior students).

'One Minute Decoder' (8)

Question 1: Acidosis or Alkalosis?

Look at pH

i. **Low pH**-----Acidosis
ii. **High pH**----Alkalosis

A. **If pH is Normal**--A normal pH does not rule out existence of an acid base disorder:

a. All three are normal –Normal Acid Base Status
b. PCO_2 and HCO_3 change grossly in the same direction ----mixed disorder of opposing type e.g. Metabolic acidosis and Respiratory alkalosis
c. Fully compensated Chronic Respiratory Alkalosis if HCO_3 decrease as per Boston equation for chronic respiratory alkalosis.

B. If pH is Abnormal

Question 2: Primary disorder is Metabolic or Respiratory??

Examine pH and HCO_3 relationship (For single disorders)

a. If pH and HCO_3 change in the same direction primary abnormality is metabolic

Examples:

- in metabolic acidosis both pH and HCO_3 decrease
- in metabolic alkalosis both pH and HCO3 increase

b. If pH and HCO_3 change in the opposite direction primary abnormality is respiratory

Examples:

- In respiratory acidosis pH decreases and HCO_3 increases
- In respiratory alkalosis pH increases and HCO_3 decreases

Question 3: Single or Double disorder???

This question requires some critical thinking. According to the primary disorder, an appropriate Boston rule is selected. Expected level of CO_2 is calculated for metabolic disorders and appropriate level of HCO_3 is calculated for respiratory disorders. The Bostonian Rules are as following:

a. Acute respiratory acidosis: Exp HCO 3= 24 + [(pCO2 − 40)/10]
b. Chronic Resp Acidosis: Exp HCO 3 = 24 + 3.5 [(pCO2 − 40)/10]
c. Acute Respiratory Alkalosis: Exp HCO 3 = 24 – 2 [(40 − pCO2)/10]
d. Chronic Respiratory Alkalosis: Exp HCO 3 = 24 – 5 [(40 − pCO2)/10]
e. Metabolic Acidosis: Exp PCO_2 = 1.5 × HCO3 + 8 (range: ±2)
f. Metabolic Alkalosis: Exp PCO_2 = 0.7 (HCO3) + 21 (range: ±2)

Figure 1: Acid Base Disorders - Animated

pH and HCO_3 Relationship

- pH and HCO3 are two friends studying in a university.
- Sometimes they are in good terms. They meet daily and go everywhere together. *'M' for 'Meet' and 'M' for 'Metabolic'*
- Other times they are not in good terms and repel each other's presence. If one goes to library, the other goes to cafeteria. *'R' for 'Repel' and 'R' for 'Respiratory'*

The Main Objections to Boston "Rules"

a. Difficult to Remember: The Boston "rules" need a lot of "rot memory" and too much 'cognitive load'
b. In my personal experience of nearly 30 years of teaching ABDs, only Winters Formula is easy to remember, so I encouraged my students to remember this formula for the metabolic acidosis [$PCO_2 = (1.5 \times HCO_3) + 8$]. By the way, Dr R.W. Winter was a Pediatrician from Columbia University, New York (Western side of Atlantic).
c. Not Stoichiometric: A big objection to these six equations was that one cannot find an amount of strong acid or base required to be added in vitro or in vivo to correct the disturbance.
d. Despite objections, these equations are hugely popular around the globe. But unfortunately "base excess" calculations have been removed in some part of the world from analyzer printouts (1).

The Copenhagen School of Thought:

The flagship parameter of Copenhagen group is 'Standard Base Excess' (SBE), but this parameter evolved gradually from 'Standard Bicarbonate' ($stHCO_3$) to 'Base Excess' (BE) and then SBE. The evolution took place in response to the objections raised from time to time from the Boston group.

Standard Bicarbonate ($stHCO_3$)

Initially devised by K Jørgensen, P Astrup in 1957, this parameter is calculated using Henderson and Hasselbeck Equation, keeping ($PaCO_2$ at 40 mmHg (9). It is still part of BGA reports, and helps the providers get an idea of presence or absence of respiratory ABD at one glance:

a. If actual HCO_3 (acHCO3) and $stHCO_3$ are close to each other, it indicates absence of a respiratory disorder.
b. If $acHCO_3$ is *lower* than $stHCO_3$, then respiratory alkalosis (compensatory decrease)
c. If $acHCO_3$ is *higher* than $stHCO_3$, then respiratory acidosis (compensatory increase)

There were two objections to this parameter:

a. The changes in [HCO_3] parameter are not stoichiometric i.e. one cannot quantitate the changes for providing treatment.
b. This parameter is developed in vitro and does not replicate in vivo pH/$PaCO_2$ relationship (1).

Base Excess:

Dr Ole Siggaard-Andersen, a Physician, and Dr Poul Astrup a Clinical Chemist, both from Copenhagen (Denmark) jointly invented the concepts of BE and SBE (10)

Definition of BE

- "Dose of acid or base required to return the pH of a blood sample to 7.40 measured at standard conditions - 37°C and 40 mmHg PaCO2".
- The purpose of this calculated parameter is to assess metabolic ABDs independent of respiratory ABDs.

Objection to BE by Boston Group

In 1963, Schwarz and Relman pointed out that BE is not CO2 -invariant in vivo. This is because for any specimen of arterial blood the in vitro plasma pH/$PaCO_2$ equilibration curve differs from the in vivo curve, since in vivo CO_2 equilibration occurs throughout the total extracellular compartment (11)

Definition of SBE

a. "Dose of acid or base required to return the pH of an anaemic blood sample to 7.40 measured at standard conditions - 37°C and 40mmHg PaCO2 calculated for a Hb of 50 g/L"
b. This parameter was devised to counter the objection on BE that it does not caters for the extra-cellular fluid (ECF) other than blood as haemoglobin buffers both the intravascular and the extravascular fluid. If blood is hypothetically mixed with other ECF, the haemoglobin will get diluted to about 50 g/L (5 g/dl).
c. Thus, SBE assesses the buffering of the whole ECF, not just the haemoglobin-rich intravascular fluid (1)

SBE Rules

Like "Boston Rules", Copenhagen Group has also developed four $PaCO_2$/SBE rules (SBE in mmol/L, $PaCO_2$ in mmHg) (12)

a. Acute respiratory acidosis and alkalosis SBE=0 x $\Delta PaCO_2$
b. Chronic respiratory acidosis and alkalosis SBE=0.4 x $\Delta PaCO_2$
c. Metabolic acidosis $PaCO_2$=SBE
d. Metabolic alkalosis $PaCO_2$=0.6 x ΔSBE

Application of SBE Rules

First determine Primary Disorder by using 'One Minute Decoder' or by directly examining $PaCO_2$ and pH (Table 1), then apply the rules mentioned above.

Table 1: Direct method of Finding Primary Acid Base Disorder

PaCO2	**pH**	**Primary processes**
Normal	Normal	None
Normal	High	Metabolic alkalosis, Respiratory alkalosis
Normal	Low	Metabolic acidosis, Respiratory acidosis
High	Normal	Respiratory acidosis, Metabolic alkalosis
High	High	Metabolic alkalosis
High	Low	Respiratory acidosis
Low	Normal	Chronic respiratory alkalosis
Low	High	Respiratory alkalosis
Low	Low	Metabolic acidosis

Novel Diagnostic BGA Interpretation Method in 2023

Dr Rajini Samuel has developed a novel method of BGA reports based on Hydrogen ion concentration. She has compared this method with Boston rules and found satisfactory correlation (13). So, Boston rules are still very much alive!!

Bostonian Rules, SBE and Copenhagen Rules in the Era of Artificial Intelligence

Presently stHCO_3, BE, SBE and Bostonian rules are widely used by the healthcare providers for the interpretation of BGA reports without having the slightest idea about 'The Great Debate'. Please consider following challenges and opportunities in BGA interpretation:

a. Imagine an Internist or Resident of specialty other than Anesthesia or Critical Care Medicine is on duty at 2:0 am in an Intensive Care Unit; a dozen patients are on ventilatory support and BGAs are carried out on hourly basis on a point-of-care-testing unit. What options he /she will have to interpret these reports? Literally very few. He / she will just make some superficial deductions about the patient condition based on his/her limited knowledge. He /she may start an insufficient or inappropriate patient treatment.
b. Can we develop algorithms for machine-learnings, so that the type of ABD, stoichiometric analysis and exact dose of the replacement or counteracting substance is instantly known?
c. Blood gas analysis is an expensive investigation requiring heavy funds even if the workload is not so much. We need to make it as meaningful as possible by adding AI in this system.
d. Lastly, almost all 'rules' classify the respiratory disorders in acute and chronic types because of delayed renal response to respiratory changes. This classification is arbitrary, blunt and discretionary. We must devise a crisp and unambiguous criteria for this division, so that AI can apply a specific rule of interpretation.

Conclusion

When you find BE, SBE, Standard HCO_3 and PCO2 and HCO3 rules, give a smile and remember 'The Great Trans-Atlantic Debate'. The present and next generations of Laboratory Specialists and Clinicians should initiate new debates , about adding Artificial Intelligence in BGA reports, so that, the future reports should contain an opinion about the acid base disorder present in the particular patient, the quantity of acid excess or deficit and calculated amount of antidote required.

References

1. T. J. Morgan. Standard Base Excess. In: Australasian Anaesthesia [Internet]. ANZCA; 2013. p. 100. Cited on 15th July 2024; Available from: https://airr.anzca.edu.au/anzcajspui/bitstream/11055/950/1/Australasian Anaesthesia 2003
2. Sadiq S, Ijaz A, Hussain M. Establishing correlation of pH with various physiochemical and traditional parameters of acid base balance: a cross-sectional study. Khyber Medical University Journal. 2022; 14(2):104–9.
3. Anzca. Australasian anaesthesia 2013. 2013; 1–119. Available from: papers2://publication/uuid/5B9A7B12-9DDF-46CE-964F-94A7611F76FE
4. Shwartz WB, Relman AS. A critique of the parameters used in the evaluation of acid-base disorders. N Engl J Med.1963; 328(8):268:1382-1388.
5. Todi S. Arterial Blood Gas Analysis: A New Look at the Old Formula. Indian Journal of Critical Care Medicine. 2023; 27(10):699–700.
6. Sood P, Paul G, Puri S. Interpretation of arterial blood gas. Indian Journal of Critical Care Medicine. 2010; 14(2):57–64.
7. Oosthuizen NM, Head A, Academic T. Approach to acid-base disorders – a clinical chemistry perspective Systematic approach. 2012; 30(7):1–8.
8. Acid Base Disorders. In: Ijaz A, editor. Lahore Chemical Pathology for the Beginners 1st Edition Azeem Sons; 2018. p. 94–8.
9. Jørgensen K, Astrup P. Standard bicarbonate, its clinical significance, and a new method for its determination. Scand J Clin Lab Invest. 1957; 9(2):122–32.
10. O.Siggaard-Andersen 1994-05-31 (revised 2004-01-25). Definition of base excess and concentration of titratable hydrogen ion: [cited 2024 Jul 17]. Anthology on Base Excess. Available from: http://www.siggaard-andersen.dk/OsaAnthologyOnBE.htm
11. Severinghaus JW. Siggaard-andersen and the “great trans-Atlantic acid-base debate.” Scand J Clin Lab Invest. 1993; 53(s214):99–104.
12. Schlichtig R, Grogono AW, Severinghaus JW. Human PaCO2 and standard base excess compensation for acid-base imbalance. Crit Care Med. 1998; 26(7):1173–9.
13. Samuel R. Application of Boston Compensation Rules in the Development of a Stepwise Approach for Novel Diagnostic Arterial Blood Gas Interpretation Method. Indian Journal of Critical Care Medicine. 2023; 27(10):717–23.

Exploring the Utility of Mitochondrial DNA Copy Number as a Quantitative Biomarker in Health and Disease

Dr. Deepak N Parchwani[1], Dr. Ragini D. Singh[2], Dr. Sagar Dholariya[3], Dr. Amit Sonagra[4]

1. Additional Professor, Department of Biochemistry; All India Institute of Medical Sciences Rajkot, Gujarat, India
2. Associate Professor, Department of Biochemistry; All India Institute of Medical Sciences Rajkot, Gujarat, India
3. Assistant Professor, Department of Biochemistry; All India Institute of Medical Sciences Rajkot, Gujarat, India

Corresponding Author
Dr. Deepak N Parchwani

Abstract

Mitochondrial DNA copy number (mtDNA-CN) refers to the total number of mitochondrial DNA molecules within a cell, which varies depending on cell type and environmental factors. This variation provides critical insights into cellular health and function. A reduction in mtDNA-CN can signal changes in the cellular environment, potentially triggered by various factors, including stress or disease. The regulation of mtDNA-CN is governed by mitochondrial replication processes and influenced by factors such as energy demand, nutrient availability, and aging.

Several methods are used to measure mtDNA-CN, including quantitative PCR (qPCR), digital PCR (dPCR), and next-generation sequencing (NGS). These techniques enable accurate quantification, although each has limitations. MtDNA-CN is increasingly recognized as a potential biomarker for various health conditions, including cancer, neurodegenerative diseases, and aging-related disorders. Research indicates that mtDNA-CN could reflect mitochondrial biogenesis, oxidative stress, or cellular aging, making it a valuable tool in disease diagnosis and monitoring.

Despite its potential, challenges remain in standardizing mtDNA-CN measurements and understanding its role in different tissues and conditions. Further research is needed to fully realize its clinical utility and to explore its implications in health and disease.

Keywords: Biomarkers, Cellular health, Mitochondrial DNA copy number, Quantification methods

Introduction

Oxidative phosphorylation (OXPHOS) takes place in the mitochondria, resulting in the production of adenosine triphosphate (ATP) following respiration. This process can cause accumulation of free radicals, resulting in the initiation of membrane lipid peroxidation and the production of human serum malondialdehyde (MDA) from these lipid hydroperoxides, where a standard colorimetric method can be used to quantify serum MDA levels. It has been

reported that systemic MDA levels are increased in diseases such as cardiovascular disease, impaired glucose metabolism, and Hashimoto's Thyroiditis, in addition to declining energy metabolism (lower OXPHOS function). The ability to measure MDA is thus a bio-indicator of either declining health or adaptation to the disease; hence, it is referred to here as a chronic'function' variable to OXPHOS levels [1]. However, the above chronic system response to declining OXPHOS does not give information on OXPHOS activity levels directly at the source, i.e. in human muscle tissue. Mitochondria have their own genetic code, i.e. mitochondrial DNA (mtDNA), which is the sole genetic source of OXPHOS enzyme production in human tissue. This is useful as mtDNA levels are not only highly variable but also have a high heritability of between 42-78% [2]. It is here proposed that mtDNA copy number (cn) in muscle can be used as a 'state' variable, reflecting OXPHOS activity levels at the source/organs of energy metabolism, particularly if analyzed with other complementary biological and physical measures.

Mitochondrial DNA Copy Number: Basics and Regulation

Mitochondrial DNA (mtDNA) copy number is comprised of the total number of mtDNA molecules within a cell and can provide valuable insights into several cellular characteristics. There is no specific "normal" or "mile" range for the copy number as it varies widely and depends mostly on the cell type and environmental factors. A decrease in copy number describes smaller differences in mtDNA, but it is vital to appreciate that these can also be triggered by other factors, such as a change in cellular environment that activates a reduction in mass. Moreover, under certain conditions like cancer in which mtDNA variations are increased, their analysis is very complex [3].

Several cellular processes are responsible for the regulation and homeostasis of mtDNA copy number. Firstly, mtDNA replication initiates at the mitochondrial displacement loop (D-loop), which is rich in replication origins. On average, it transcribes and replicates single-stranded RNA and DNA strands that compete for initiating replication. Secondly, mtDNA replication is affected by a multitude of physical and cellular characteristics. High energy in cells in a hypoxic state will be expended in the generation of ATP, glycine, and fumarate, leading to depletion of the inhibiting nucleosides and the mitochondrial replication restart. Additionally, the electron transport chain of a cell's mitochondria is affected by exogenous and endogenous changing properties like nutrients, environment, and age have affected or can affect mitochondrial copy number [4, 5].

Mitochondrial DNA copy number (mtDNA-CN) is increasingly making headway as a potential marker for several conditions affecting human health and behaviour. This review aimed to illuminate the knowledge surrounding mtDNA-CN in normal and diseased states in humans.

Methods for Measuring Mitochondrial DNA Copy Number

The quantitative assessment of mtDNA copy number holds significant importance in understanding various physiological and pathological processes. The measurement of mtDNA copy number is essential for investigating cellular responses, disease progression, and therapeutic interventions. There are a variety of techniques and strategies to quantify mitochondrial DNA copy number as a quantitative biomarker, and it is important to understand the ways to perform such measurements in order to interpret the evidence. The limitation of a given method needs to be considered in the execution and results interpretation, to assess correctly mitochondrial DNA copy number's role in biological and pathological processes.

quantitative PCR (qPCR): qPCR has now become the most widely used technique for determination of mitochondrial DNA copy number because it is rapid, reliable, easy to perform, and generally less time-consuming compared with other methods. More importantly, qPCR allows to quantify the mitochondrial DNA copy number identified as the ratio of two DNA molecule distributions (mitochondrial DNA and nuclear DNA) using calibration curves. qPCR standard curve should be generated using a serial dilution of human mitochondria and nuclear DNA for estimating the absolute amount of gene of interest [6]. However, qPCR's reliance on standard curves can introduce variability, and it may not distinguish between different mtDNA populations.

Digital PCR (dPCR) has emerged as a robust technique for quantifying mitochondrial DNA (mtDNA) due to its unique attributes. Unlike traditional PCR, dPCR partitions the sample into thousands of individual reactions, allowing for absolute quantification of DNA molecules.

Digital PCR (dPCR) has emerged as a robust technique for quantifying mitochondrial DNA (mtDNA) due to its unique attributes. Unlike traditional PCR, dPCR partitions the sample into thousands of individual reactions, allowing for absolute quantification of DNA molecules.

The utilization of EvaGreen in dPCR experiments has been shown to reliably quantitate mtDNA copy number by directly using cell lysates, eliminating the need for a nuclear reference gene and reducing compounded errors. This method has demonstrated the ability to detect subtle changes in mtDNA levels, making it particularly relevant for analyzing differences in mtDNA content between cell states and pathological conditions.

The dPCR method's performance surpasses many prevalent quantitative methods, making it an affordable and powerful tool for quantifying genetic material and serving as a non-invasive biomarker for various diseases.

Next-generation sequencing (NGS) has revolutionized the analysis of mitochondrial DNA (mtDNA) copy number by enabling highly sensitive detection of low-level mtDNA variants. To ensure accurate variant calling and avoid false positives induced by nuclear mitochondrial DNA sequences (numts), it is crucial to enrich the DNA sample for mtDNA. One commonly used method for mtDNA enrichment is the differential centrifugation (DC) technique, which allows for abundant mitochondrial isolates. However, the harsh nature of high-speed centrifugation in DC can lead to disruptions and potential nuclear DNA contamination. An alternative approach involves the use of magnetic bead isolation, which yields whole mitochondria with intact membrane machinery and reduces contamination compared to DC. Additionally, amplification of the mitochondrial genome using long-range PCR with one to two primer pairs is frequently employed for mtDNA sequence enrichment.

Furthermore, next-generation sequencing (NGS) offers the advantage of absolute quantification, which provides a simple method to calibrate optical measures of mtDNA copy number in single cells, as demonstrated by the mCN assay. This precise quantification capability enhances the accuracy of mtDNA copy number analysis and expands the potential applications of NGS in this context.

Mitochondrial DNA Copy Number in Health and Disease

Mitochondrial DNA (mtDNA) copy number (mtDNAcn) has emerged as a robust quantitative biomarker, and normative reference range values are becoming established. Expression

values and various parameters of inflammation either do not or only account for a fraction of the variance in mtDNAcn. While an appreciable fraction of the between-subject variance in some somatic tissues, such as whole blood mtDNAcn, is the result of random variation across cell types in a population, somatic tissue mtDNAcn estimations are generally reproducible for an individual over time in nonpathological states. Additionally, some mtDNAcn alterations have been consistently found to be characteristics of a cell or tissue [7]. Thus, tissue mtDNAcn can be measured in some cases to estimate the relative latitudinal (and/or chronological) age of a tissue.

Along with age, mtDNAcn has been linked to several human health outcomes and is a subject of active research in many diseases. In some cases, there is compelling evidence for a link between mtDNAcn and neurodegenerative diseases, cancer, and possibly other diseases associated with inflammation and metabolism. A potential utility of mtDNAcn is as an intermediate in knowledge discovery and validation of diseases suspected to have an inflammatory or metabolic component. Associations with cancer have generated considerable interest. Of particular interest concerning these articles is data indicating that mtDNAcn can be quite dynamic in whole tissues, or at least in blood. This is consistent with experimental data generated in cell culture and transgenic animals demonstrating that mtDNAcn changes in response to experimental treatments. In tissues, more cells may be obsolescent than in particular cell types, suggesting that both mtDNAcn and the utility of association analyses based on mtDNAcn may vary by tissue [8].

Mitochondrial DNA Copy Number in Aging

In the last 5 years, there has been a substantial number of publications that attempt to understand this parameter in a diverse range of tissues, in health and disease, and at different life stages. The work can be broadly categorized into that which is concerned with events of aging, its relatedness to any changes in commensal or adaptive mitochondrial biogenesis, and, if it is also altered with membrane potential, whether changes might contribute or result from the aging or disease process. Alternatively, some papers have approached the same subject concerned with falling solely under the aging process, representing a biologically predetermined mitochondria-to-cell number, the cause of which has not always been attributed to a functional or adaptive basis [9].

The published progression/correlation of mtDNA copy number with age has been in relation to either one or a combination of such factors as a surrogate marker of mitochondrial number, a reflection of mitochondrial biogenesis, results of oxidative stress, possible autophagy or mitophagy, or an adaptation to a decline in membrane potential. The observation of interindividual variation in mtDNA copy number has led to their determination in a variety of easily obtainable or accessible tissues, to identify their relationship with age and the variance of such numbers in the same samples or tissues from patients with diseases known to be either associated with pregnancy or preceding the development of aging/disease [10]. Further studies have also used mtDNA copy number to investigate tissue- or gender-associated differences in blood samples. However, the increasing amount of work now published means that it is also timely to question their utility - why of relevance? And what do they tell us about our biology?

Mitochondrial DNA Copy Number in Neurodegenerative Diseases

Research into the involvement of mtDNA copy number in neurodegenerative diseases (ND) is recent, but the mitochondrial theory of aging has implicated mtDNA mutation and content

status in age-related ND. This accumulation of damage to mtDNA can lead to a reduction in mtDNA copy number and increase the susceptibility of cells and tissues to undergo cell death. This association has only recently been considered an avenue of research to explore whether mtDNA copy number alone or as part of a ratio could be used as a marker of the pathophysiological mechanism of NDs [11]. Numerous studies demonstrate reductions in mtDNA copy number in common ND pathologies, behaviours, or symptomology.

Among Alzheimer's disease, the majority of studies report decreases in mtDNA copy number, even using different tissue samples. There are, however, exceptions to this finding. Within the blood, reports are mixed with elevations also being reported. In other NDs, reductions in mtDNA copy number are observed within HD and PD pathologies. Within the blood, the reduction is more consistent and found in PD and ALS. The multitude of reports across the interconnected NDs propel further inquiry to understand the potential of mtDNA copy number as a useful marker of metabolic activity during ND [3]. The explorative nature of these studies also implies that mtDNA copy number should be used as a quantitative measure aid for other well-established markers, even when no differences in ND are reported.

Mitochondrial DNA Copy Number in Cancer

An increasing number of studies have reported that mitochondrial DNA copy number is more likely to increase in cancer tissues and that it is frequently increased in many types of cancer. It has been shown that higher levels of mitochondrial DNA copy number are present in solid tumors compared to corresponding non-tumor tissues. Compared to healthy controls, cancer patients have a higher mtDNA copy number in peripheral blood leukocytes, subsequently conferring to be an important predictor for cancer diagnosis. However, increased levels of mtDNA copy number have also been associated with a poorer outcome [12]. These variations in the mode of regulation of mitochondrial DNA content across different cancer types strongly suggest the relevance of mitochondrial DNA. Additionally, recent evidence shows that mtDNA copy number levels are affected by inherited polymorphisms.

In conclusion, although mitochondrial DNA copy number measurements highlight both the direct influence and contribution of mitochondrial content in cancer, the value of mtDNA copy number likely goes beyond only cancer. Mitochondrial DNA copy number can be easily assessed using easy-to-use biological materials, including circulating cell-free DNA, resulting in its promising role as a biomarker of disease and therapy response, supporting the strong interest and potential role in oncology for the future. More investigations are required to standardize mtDNA copy number analysis and interpretation in the clinic.

Challenges and Limitations in Using Mitochondrial DNA Copy Number as a Biomarker

Measuring variation in mitochondrial DNA (mtDNA) copy number has potential utility as a representational or quantitative biomarker. If mtDNA copy number can serve as a quantitative indicator of mitochondrial abundance or incorporation of mtDNA into the nuclear DNA of actively copying cells, mitochondrial parameters should be related to it. There are two reasons to be cautious of this association, and to consider alternative means to define mtDNA depletion in tissue: (1) diseased and control tissue can have different amounts of cellular heterogeneity in the distributions of mitochondrial and nuclear genes per cell; and (2) tested clinical phenotypes and sequences, all mRNA collected post-mortem from human middle frontal cortex, differ

Furthermore, inherent and induced heterogeneity among human tissues in mitochondrial and nuclear gene copy number per cell will not give identical relative levels of mtDNA and nuclear DNA with mitochondrial deletions (and without experimental depletion), and thus make mtDNA copy number of limited interest as a quantitative biomarker. Although mtDNA copy number is described in the human research literature as a measure of cellular and biological function, it does not rise to the rank of an established qualitative biomarker to track mitochondrial proliferation during muscle aging, disease, or adaptive remodeling, let alone a quantitative biomarker to match numbers against the severity of disease manifestation. A mathematical model can help differentiate whether a difference in the published results reflects a solution to differences of tissue or tissue pathologies, as opposed to differences in the emphasis given to one out of four alternative ways of estimating the copy number ratio. To sum up, while a pure- or skeletal muscle-derived mtDNA copy probably will not be useful as an ameliorative outcome biomarker from the research perspective, an mtDNA copy number may supplement measures of the rate of injury in a clinical context.

Conclusion

Mitochondrial DNA copy number has primarily been utilized as an outcome measure in human studies that are exploring mitochondrial biogenesis, life course epidemiology, aging, cell death, mitochondrial and nuclear DNA damage, or the association with one of a selection of common diseases and conditions. The evidence suggests that many of these will be relevant and that there is potential in this field of research, but current methodology and design in association with this fairly new field require substantial further work to achieve routine clinical use. There is a growing body of genetic studies in this area, which is mainly based on common variation and has not identified any single-nucleotide polymorphism that, aside from TFAM, is associated with levels of mitochondrial DNA copy number of the nuclear genome. No longitudinal studies in terms of genetic factors have been done, but it is clear that the association with mitochondrial DNA copy number is complex and is likely to contain many loci for differing physiological processes.

Environmental factors that are also thought to influence the copy number include drugs that cause mitochondrial toxicity, and heavy metals, especially lead. Replication of the genetics associations and some gene-environment causal inference fields in humans will result in a genetics-environment field and improve our understanding of the mitochondrial genome and the copy number in health and disease. The conclusion on utility is that copy number has potential, but the research is currently purely hypothesis generating. If health can be improved by maintaining the copy number, then health interventions to achieve the desired level could be imagined. In some diseases, the research into copy numbers is at the departure stage to health. In other areas, the research is certainly already of interest in terms of disease, particularly to tumors. That change in copy number or the absolute level reports on the level of damage in terms of apoptosis, or that an altered absolute level of copy number compared to the rest of the population might be a risk factor in cancer. The difference in the absolute level of copy number does, by the consensus of the field, not cause cancer but appears to be of interest as a field sensor.

References:

1. Longchamps RJ, Castellani CA, Yang SY, Newcomb CE, Sumpter JA, Lane J, Grove ML, Guallar E, Pankratz N, Taylor KD, Rotter JI. Evaluation of mitochondrial DNA copy number estimation techniques. PloS one 2020 Jan 31; 15(1):e0228166.

2. Lin YH, Lim SN, Chen CY, Chi HC, Yeh CT, Lin WR. Functional role of mitochondrial DNA in cancer progression. International journal of molecular sciences. 2022 Jan 31; 23(3):1659.

3. Yang SY, Castellani CA, Longchamps RJ, Pillalamarri VK, O'Rourke B, Guallar E, Arking DE. Blood-derived mitochondrial DNA copy number is associated with gene expression across multiple tissues and is predictive for incident neurodegenerative disease. Genome research. 2021 Mar 1; 31(3):349-58.

4. Misic J, Milenkovic D, Al-Behadili A, Xie X, Jiang M, Jiang S, Filograna R, Koolmeister C, Siira SJ, Jenninger L, Filipovska A. Mammalian RNase H1 directs RNA primer formation for mtDNA replication initiation and is also necessary for mtDNA replication completion. Nucleic Acids Research. 2022 Aug 26; 50(15):8749-66.

5. Liu Y, Liu H, Zhang F, Xu H. The initiation of mitochondrial DNA replication. Biochemical Society Transactions. 2024.

6. Leuthner TC, Hartman JH, Ryde IT, Meyer JN. PCR-based determination of mitochondrial DNA copy number in multiple species. Mitochondrial Regulation: Methods and Protocols. 2021:91-111.

7. Picard M. Blood mitochondrial DNA copy number: what are we counting? Mitochondrion. 2021.

8. Kopinski PK, Singh LN, Zhang S, Lott MT, Wallace DC. Mitochondrial DNA variation and cancer. Nature Reviews Cancer. 2021 Jul; 21(7):431-45.

9. To KK, Cheng VC, Cai JP, Chan KH, Chen LL, Wong LH, Choi CY, Fong CH, Ng AC, Lu L, Luo CT. Seroprevalence of SARS-CoV-2 in Hong Kong and in residents evacuated from Hubei province, China: a multicohort study. The Lancet Microbe. 2020 Jul 1; 1(3):e111-8.

10. Kang JI, Park CI, Lin J, Kim ST, Kim HW, Kim SJ. Alterations of cellular aging markers in obsessive–compulsive disorder: mitochondrial DNA copy number and telomere length. Journal of Psychiatry and Neuroscience. 2021 Jul 1;46(4):E451-8.

11. Bazzani V, Equisoain Redin M, McHale J, Perrone L, Vascotto C. Mitochondrial DNA repair in neurodegenerative diseases and ageing. International Journal of Molecular Sciences. 2022 Sep 27; 23(19):11391.

12. Abd Radzak SM, Mohd Khair SZ, Ahmad F, Patar A, Idris Z, Yusoff AA. Insights regarding mitochondrial DNA copy number alterations in human cancer. International Journal of Molecular Medicine. 2022 Jun 16;50(2):104.

Lead Poisoning in Nepal: Unveiling the Rising Concern and Shaping Future Policies

Prepared by: Dr. Vivek Pant

Consultant Biochemist and Head- Research Unit, Samyak Diagnostic Pvt Ltd, Kathmandu, Nepal.
Corresponding member, Communication and Publication division, APFCB.
Corresponding member, Task Force Young Scientist, IFCC.
Corresponding member, Task Force on Outcome Studies in Laboratory Medicine, IFCC.

Background

Writing this special report on lead poisoning was prompted by my observation of numerous cases with exceptionally high blood lead levels during the past years. Upon further investigation, I found that some of these individuals were consuming herbal supplements, while others were beauticians frequently using cosmetics. Additionally, a child who regularly played with shiny plastic toys was also affected. Notably, all these cases of lead poisoning presented with acute abdominal pain. The extent of the issue is likely to be significant, as these findings originate from a single center and lead levels in potential causative agents have not been measured. Furthermore, there is a lack of awareness among healthcare providers in Nepal, highlighting an urgent need for comprehensive investigation and policy development to address this public health concern.

Statement of Problem

Lead exposure remains a critical public health challenge in Nepal due to its widespread presence in the environment. Major sources include -

1. Traditional Medicine- Ayurvedic Medicine (1)
2. Industrial Emissions- Factories and industries that use lead in their processes can release lead into the environment.(2)
3. Household Items- Lead-based paints and plumbing systems can contribute to lead exposure.(3)
4. Improper disposal and handling of electronic waste (4)
5. Environmental Contamination- Leaded gasoline, although phased out, has left a lasting legacy of lead in soil and dust.
6. Toys - Regardless of regulatory limits on the content of lead, children's toys existing in Nepal has high lead content.(5)
7. Cosmetics: Nepal does not have any standards, guidelines, or legislation regarding the limits of heavy metals in cosmetic products. Neither government agencies nor private sectors monitor the heavy metal impurities in cosmetics imported, produced, marketed, distributed, and used in Nepal. (7)

The pervasive nature of lead in the environment poses a serious threat to public health, particularly affecting children, who are more susceptible to lead poisoning. A recent study has shown that 64% of children between 6-36 months in Nepal have detectable blood lead level.(7) Lead exposure in children can lead to developmental delays, cognitive impairments, and various health issues, creating an urgent need for comprehensive strategies to reduce and manage lead contamination in Nepal.

Diagnostic Challenges

Diagnosing lead poisoning is fraught with challenges, including:

1. **Nonspecific Symptoms**: Lead poisoning symptoms often mimic other illnesses, making it difficult to diagnose based on clinical presentation alone. Symptoms such as abdominal pain, irritability, fatigue, and developmental delays in children can be easily attributed to other conditions.
2. **Lack of Awareness**: Many healthcare providers in Nepal may not consider lead poisoning in their differential diagnoses due to a lack of awareness and training on the issue.
3. **Limited Access to Testing**: Even when lead poisoning is suspected, access to reliable diagnostic testing is limited. This is exacerbated by the scarcity of laboratories equipped to measure blood lead levels accurately.
4. **Overlooking by healthcare providers:** In resource-limited settings, clinicians may prioritize more immediate health concerns over lead poisoning, especially if it is perceived as less common or less urgent.

Call to Action

1. **Inclusion in Essential Diagnostics List**: The World health organization (WHO) should consider including lead testing in the essential list of diagnostic tools. This would ensure global recognition of the importance of lead testing and encourage its adoption in national health systems.
2. **Increase awareness and educational events**: Concerned authorities should support initiatives aimed at raising awareness about lead poisoning among healthcare providers and the general public. Continuous professional development programs for medical professionals on the diagnosis and management of lead poisoning are essential.
3. **Support for Laboratory Infrastructure**: International organizations should assist Nepal and the region in building and equipping laboratories capable of performing accurate lead testing. This includes providing technical support, funding, and resources.
4. **Policy Advocacy**: Advocating for policies that reduce lead exposure, such as regulations on industrial emissions, paints and cosmetics, safer practices in traditional medicine, and public health campaigns, is critical.

Role of APFCB - Establishing an APFCB Working Group for blood lead level to enhance early detection and prevention in developing nations:

The APFCB should consider establishing a dedicated working group focused on blood lead level testing in developing nations within the region. This group could play a crucial role in advocating for comprehensive screening models, promoting the adoption of point-of-care testing (POCT) devices, and pushing for the inclusion of BLL tests on the World Health Organization's essential list of in vitro diagnostics.

By promoting these initiatives, the working group can help improve early detection and management of lead poisoning, a significant public health issue in many developing countries. Furthermore, the group could foster scientific research aimed at better understanding the sources, epidemiology, and preventive strategies for lead exposure, ultimately contributing to the reduction of lead poisoning incidents. This coordinated effort would not only enhance diagnostic capabilities but also support policy development and implementation, ensuring that effective lead poisoning prevention and intervention measures are in place across the Asia-Pacific region.

Conclusion

Lead poisoning remains a significant but often overlooked public health issue in Nepal and the region. Addressing this challenge requires a multifaceted approach, including better diagnostic capabilities, increased clinician awareness, and stronger laboratory infrastructure.

References

1. Pant V, Gautam K, Pyakurel D, Shrestha A, Pradhan S, Joshi N. Broadening the list of differential diagnosis for acute abdomen–a case report from Nepal. EJIFCC. 2020 Nov;31(4):347.
2. Gautam K, Pradhan S, Thuppil V, Pyakurel D, Shrestha A. Blood lead level among school children in an industrial city of Nepal. Journal of Pathology of Nepal. 2017 Mar 30;7(1):1091-4.
3. Gottesfeld P, Pokhrel D, Pokhrel AK. Lead in new paints in Nepal. Environmental research. 2014 Jul 1; 132:70-5.
4. Gautam K, Pant V, Pradhan S, Pyakurel D, Bhandari B, Shrestha A. Blood lead levels in rag-pickers of Kathmandu and its association with hematological and biochemical parameters. EJIFCC. 2020 Jun; 31(2):125.
5. Suwal A, Prajapati M, Shah RC. Assessment of Toxic Heavy Metal Content in Children Toys. Khwopa Journal. 2023 Dec 29; 5(2):147-62.
6. Dangi NB, Maharjan S, Shrestha A, Rokaya RK, Joshi KR. Determination of heavy metals in selected cosmetic products sold in Nepal. Journal of Health and Allied Sciences. 2022; 12(2):23-7.
7. Dhimal M, Karki KB, Aryal KK, Dhimal B, Joshi HD, Puri S *et al*.High blood levels of lead in children aged 6-36 months in Kathmandu Valley, Nepal: A cross-sectional study of associated factors. PLoS One. 2017 Jun 12;12(6):e0179233.

Case-1: Preanalytical Challenges in Tacrolimus Monitoring

Author:

Dr. Vivek Pant[1] MD Clinical Biochemistry, Email: drvpant@gmail.com
Dr. Santosh Pradhan[2] MD Clinical Biochemistry, Email: drsantosh.samyak@gmail.com
[1, 2] Department of Clinical Biochemistry, Samyak Diagnostic Pvt Ltd, Kathmandu, Nepal

Summary

A 37-year-old woman experienced a significant increase in blood tacrolimus levels after starting Clarithromycin for an H. Pylori infection. Tacrolimus, used in organ transplant patients, has a narrow therapeutic index requiring close monitoring. The concurrent use of Clarithromycin, a CYP3A4 inhibitor, led to a dramatic spike in tacrolimus levels, causing signs of potential toxicity, such as elevated serum creatinine. This case highlights the critical importance of awareness of drug-drug interactions, especially involving CYP3A4 inhibitors, to prevent adverse effects and ensure patient safety. Clinicians should closely monitor tacrolimus levels when prescribing such medications.

Keywords- CYP3A4; Tacrolimus; Clarithromycin; Drug Interaction

Introduction

Tacrolimus is an immunosuppressive drug that inhibits T-lymphocyte activation by inhibition of the phosphate activity of calcineurin. It is highly bound to the erythrocytes. Absorption from the gastrointestinal tract is variable and irregular. Peak blood concentrations are achieved at 1.5 to 3.5 hours. The elimination half-life from whole blood is about 11 hours in transplant patients. It has a narrow therapeutic index range; high tacrolimus concentrations are associated with toxicity, whereas low concentrations are associated with an increased risk of graft rejection. Although dose adjustments based on therapeutic drug monitoring are performed, unexpected large variations in tacrolimus concentration are sometimes encountered.

Case Presentation

We received a request from physician to recheck blood tacrolimus level for a 37 years lady who received renal transplantation 8 years back. Her blood tacrolimus level was 36.7µg/L and on rerunning the same sample, the result was 36.1µg/L. We informed the same result to the physician. However, physician admitted his disagreement with the report because he had not increased the dosage for tacrolimus and requested for repeating the test in new sample next day. On the subsequent day, the blood tacrolimus level was 39.8µg/L and there was also rise in serum creatinine to 1.5 mg/dl which was 1.0 mg/dl 2 weeks back. Physician was informed about the result.

Careful inspection for potential source of error in all analytical steps was done. We receive around 350 blood tacrolimus samples in a month at our center. We measure blood tacrolimus using Abbott Architect i1000 (Abbott, USA). Architect tacrolimus assay is designed to have a correlation coefficient of 0.90 for samples with result between 2.0 - 30.0 µg/L when compared to LC/MS/MS.

The reagent, calibrator, internal quality control graphs and instrument were checked to identify presence of any analytical error, however no abnormality was found. There was no recent maintenance of instrument and no issues with other parameters. We confirmed the delta check for tacrolimus results in other patients and none of them were suspicious.

We decided to inquire directly with the patient. There was no change in tacrolimus dosage and any recent major illness or hospital admission. Patient denied changing the brand for tacrolimus and confirmed that she provided blood samples on empty stomach 15 minutes before her next dosage. There was no history of biliary disease and recent diarrhea which are known to increase trough tacrolimus level. On further inquiring she admitted that she was recently prescribed triple therapy by the different physician for *H.Pylori* infection after her urea breath test was positive. The therapy consisted amoxycillin 1 grams twice day, clarithromycin 500 mg twice a day and pantoprazole 40 mg twice a day for 14 days. We reviewed the literature and found that there were few case reports on drug-drug interaction between tacrolimus and clarithromycin. After contacting physician, clarithromycin was stopped and azithromycin was initiated. The subsequent blood tacrolimus dropped down to 23.1 µg/L and to 4.0µg/L within 4 days after stopping clarithromycin (Figure 1). The result-date graph (Figure 1) is directly taken from the laboratory information system.

Discussion

Tacrolimus inhibits T-lymphocyte activation by binding to an intracellular protein, FKBP-12 and complexes with calcineurin dependent proteins to inhibit calcineurin phosphatase activity. Its metabolism is mediated by cytochrome CYP3A 4/5 thus making it potential substrate for clinically significant interaction. Clarithromycin is a macrolide antibiotic used for H.Pylori eradication and is a potent CYP3A inhibitor. A reversible rise in trough concentration in tacrolimus level, due to pharmacokinetic interaction with clarithromycin, associated with nephrotoxicity as evidenced by temporary rise in serum creatinine is presented in the index case. Wolter et al. reported the first case of tacrolimus-clarithromycin interaction where a renal transplant patient whose tacrolimus level increased from 9 to 29 ng/ml 3 days after the initiation of oral clarithromycin 500 mg twice daily for suspected pneumonia. (1)

The index patient had mild nephrotoxicity owing to sudden rise in serum tacrolimus level that led to temporary increase in serum creatinine. However no other toxicity was recorded. Many factors contribute to the development of tacrolimus nephrotoxicity which includes exposure to metabolites of tacrolimus, local renal P-glycoprotein and renin angiotensin system activation resulting in vasoconstriction of the afferent and glomerular arterioles. (2) Since tacrolimus use is typically in combination with other immunosuppressant's, target levels usually decrease as post-transplant time increases to minimize calcineurin inhibitor-mediated nephrotoxicity and adverse effects. There was alarming rise in tacrolimus level in our patient after 8 years of transplant which raised concern from the physician.

CYP3A 4/5 genetic polymorphism are widely accepted to play an important role in tacrolimus metabolism and its allele mutation might be different in different races. Therefore, tacrolimus toxicity and interaction with other drugs differs among races. For an example CYP3A-5 genotype dependent drug interaction was found between tacrolimus and nifedipine in Chinese renal transplant patient. (3) Therefore personalized therapy accounting for CYP3A4/5 genotype detection as well as therapeutic drug monitoring is necessary for renal transplant patients.

After diagnosis of clarithromycin induced tacrolimus toxicity, physician advised to use azithromycin, another macrolide antibiotic, which is an alternative to clarithromycin because this antibiotic has a very similar microbiological spectrum and it does not interact significantly with CYP 3A4 enzyme. Therefore, clinicians should be aware that other drugs which are metabolized via the same enzyme system should also be used with caution for patients on tacrolimus (Table 1). (4, 5)

Conclusion

Vigilant monitoring and awareness of tacrolimus drug interaction is essential to prevent its toxicity with its narrow therapeutic window.

Acknowledgement

None

References

1. Wolter K, Wagner K, Philipp T, Fritschka E. Interaction between FK 506 and clarithromycin in a renal transplant patient. European journal of clinical pharmacology. 1994 Sep; 47:207-8.
2. Bentata Y. Tacrolimus: 20 years of use in adult kidney transplantation. What we should know about its nephrotoxicity. Artificial organs. 2020 Feb; 44(2):140-52.
3. Yang Y, Huang X, Shi Y, Yang R, Shi H, Yang X, Hao G, Zheng Y, Wang J, Su L, Li Y. CYP3A5 genotype-dependent drug-drug interaction between tacrolimus and nifedipine in Chinese renal transplant patients. Frontiers in Pharmacology. 2021 Jul 5;12:692922.
4. Van Gelder T. Drug interactions with tacrolimus. Drug safety. 2002 Aug;25:707-12.
5. Baxter K, Baxter P, Claire, L. Immunosuppressant monograph: Stockley's drug interactions 10th ed. 2013

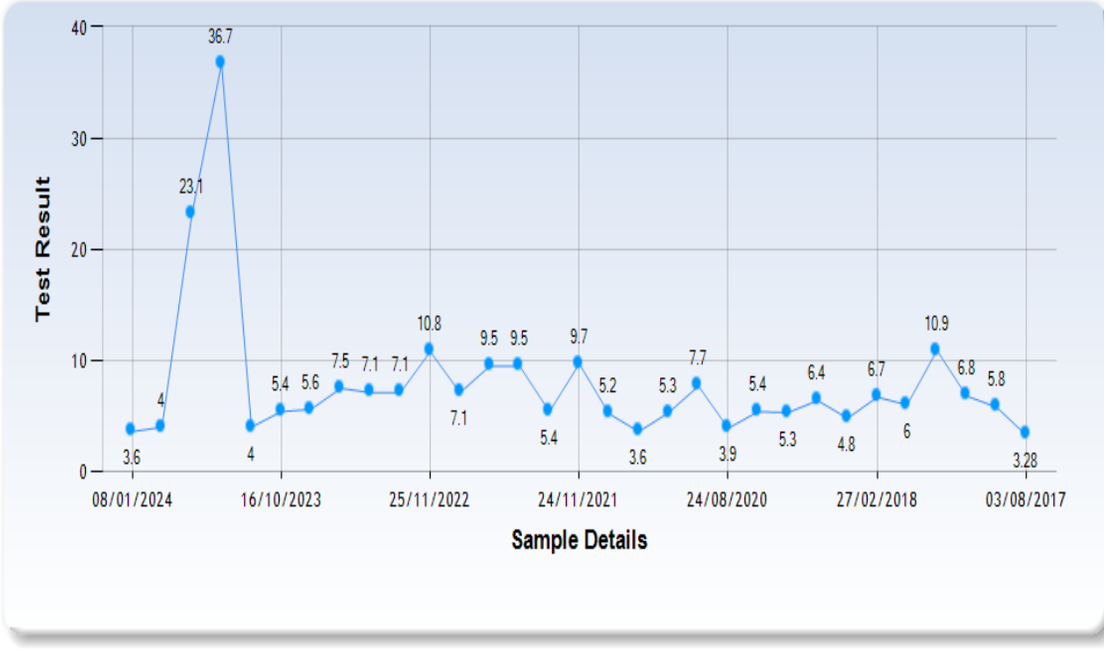


Figure 1: Tacrolimus (Y-axis) level versus date of test (X-axis)

Table 1: Drugs having interaction with Tacrolimus

Drug that increase Tacrolimus level: Inhibitor of Metabolism		**Drug that decrease Tacrolimus level: Inducer of Metabolism**	
Calcium Channel Blocker	Verapamil Diltiazem	**Antitubercular agents**	Rifampicin
Antifungal	Ketoconazole Itraconazole Fluconazole	**Anticonvulsant**	Phenytoin Barbiturates Carbamazepine
Macrolides	Clarithromycin Erythromycin	**Herbs**	Saint John's Worth (Hypericum perforatum)
Protease inhibitor	Ritonavir Indinavir	**Others**	Cinacalcet Bosentan
Fruit	Grapes		

Case 2: Hypokalaemia in Metabolic Acidosis

Author: Gusti Ayu Mardewi, Ngoerah Hospital, Bali, Indonesia, E-mail: ayumardewi6@gmail.com

Case History

Analyte	Result	Reference Interval
Sodium	138 mmol/L	135 – 145
Potassium	1.51 mmol/L	3.5 – 5.1
Chloride	107.6 mmol/L	94 – 110
Urea nitrogen	13.1 mg/dL	7-18.7
Creatinine	0.7 mg/dL	0.57-1.11
e-GFR	111.9	≥90
Arterial blood gas		
pH	7.33	7.35-7.45
pCO2	30 mmHg	35.00-45.00
pO2	75 mmHg	80.00-100.00
Bicarbonate	15.8 mmol/L	22.00-26.00
Potassium	1.2 mmol/L	3.5-5.1

Questions

1. What is the most critical result?
2. What possibilities could you offer to explain the potassium result?
3. What are the causes of hypokalaemic in metabolic acidosis?
4. Are there any other tests you might perform to clarify the likely cause of the low potassium result?

Discussion

Question 1

The most critical result is the potassium level. Very low potassium levels (less than 2.5 mmol/L) can be life-threatening and require immediate medical attention. Significant muscle weakness occurs at serum potassium levels below 2.5 mmol/L. It is an ascending pattern affecting the lower extremities, progressing to involve the trunk and upper extremities and potentially progressing to paralysis. Affected muscles can include respiratory muscles, which can lead to respiratory failure and death. Severe hypokalaemia can also lead to various cardiac dysrhythmias.

Question 2

Hypokalaemia can be caused by an intracellular shift of potassium, a decrease in potassium intake, and an increase in potassium output. Some causes of hypokalaemia can usually be determined through patient history, such as hypokalaemia due to vomiting, diarrhea, or diuretic use. However, in some cases, the cause may not be apparent, and establishing a diagnosis can be challenging (1). The cause of transient hypokalaemia may be due to a shift of potassium into the cells, while ongoing hypokalaemia may be due to insufficient potassium intake or excessive potassium loss. Excessive potassium loss can result from disorders in the kidneys or outside the kidneys (1, 2).

Question 3

The combination of hypokalemia and normal anion gap metabolic acidosis can be caused by renal and extrarenal losses of potassium and bicarbonate. The most common extrarenal causes are from the gastrointestinal tract in the presence of diarrhea and vomiting and the use of diuretics. Renal causes of hypokalaemia in a normal anion gap metabolic acidosis can be due to renal tubular acidosis, diabetic ketoacidosis, use of medications such as amphotericin B and acetazolamide. The approach to hypokalemia patients with metabolic acidosis can use a flowchart based on Figure 1.

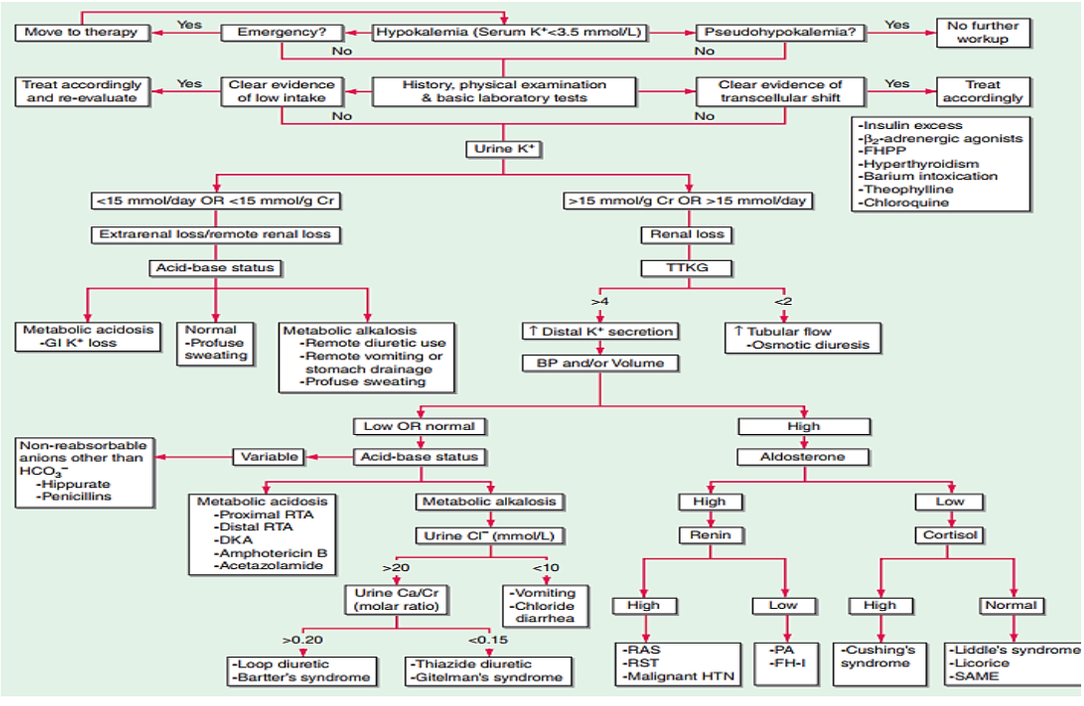


Figure 1. Approach to patients with hypokalaemia and metabolic acid-base disorders (1).

Question 4

The approach to differentiate between renal and extra-renal causes of hypokalemia can be made by measuring potassium excretion in a 24-hour urine sample or looking at random urine potassium concentration values. If the urine potassium concentration exceeds 15 mmol/day, this suggests a renal disorder as the cause. Conversely, if the urine potassium concentration is less than 15 mmol/day, there may be an extra-renal cause (1).

Assessment of potassium excretion in urine can also be done using Trans-tubular Potassium Concentration Gradient (TTKG) calculation. The trans-tubular Potassium concentration Gradient provides an estimation of potassium levels in the tubular fluid, especially at the end of the cortical collecting duct. The cortical collecting duct is the last place where potassium levels in urine are determined. The TTKG formula used is based on several references: (3, 4).

$$\mathbf{TTKG} = \frac{\mathbf{K^+(urine)x\ Osmolality\ (serum)}}{\mathbf{K^+\ (serum)x\ Osmolality\ (urine)}}$$

The following diagnostic steps performed in patients with hypokalemia are blood pressure checks and assessment of acid-base status to narrow down the differential diagnosis.

If renal tubular acidosis is suspected, additional laboratory tests, such as plasma anion gap, are performed. The plasma anion gap is the calculated result between cations and anions in plasma (including sodium, potassium, chloride, and bicarbonate) (5). Examination of urine NH4+ excretion can be used as the next step to establish the diagnosis of possible RTA. NH4+ excretion tends to be high in extrarenal loss and low in RTA. Although clinical laboratories do not routinely measure urine NH4+ levels, estimation of NH4+ excretion can be done by calculating the anion gap of urine (AGU) (1). After calculating the urine anion gap to narrow down the differential diagnosis, urine pH is examined (6, 7).

References

1. David. Fluid and Electrolyte Disturbance. In: Harrison R, Wintrobe, Thorn, Adams, Beeson, IBennett., editor. Harrison's Principles of Internal Medicine. 21 ed. United state: McGraw-Hill Education; 2022. p. 348-52.

2. Palmer BF, Clegg DJ. Physiology and pathophysiology of potassium homeostasis. Advances in physiology education. 2016.

3. Robson L. The kidney–an organ of critical importance in physiology. The Journal of physiology. 2014;592(Pt 18):3953.

4. Lin S-H. A practical and pathophysiologic approach to hypokalemia. Hong Kong Journal of Nephrology. 2008;10(1):14-26.

5. Berend K. Review of the diagnostic evaluation of normal anion gap metabolic acidosis. Kidney Diseases. 2017;3(4):149-59.

6. Soriano JR. Renal tubular acidosis: the clinical entity. Journal of the American Society of Nephrology. 2002;13(8):2160-70.

7. Desai SP. Approach to The Patient with A Normal Anion Gap Metabolic Acidosis. In: Desai SP, editor. Clinician's Guide to Laboratory Medicine A Practical Approach. 3 ed. Hudson: Lexi Comp; 2004. p. 299-305.

Quiz Section!!

Question

The following serum lab data was obtained from blood samples taken from the same individual but using different test tubes (five types). Based on the measured values, determine which data corresponds to which test tube. Tube A is a normal test tube for serum analysis. Tubes B-D contain either sodium fluoride plus EDTA-2K, sodium citrate, lithium heparin, or EDTA-2K.

Analyte	Unit	Method	Measured values				
			Tube A	Tube B	Tube C	Tube D	Tube E
TP	g/dL	Biuret	8.0	8.3	8.3	8.2	7.4
ALB	g/dL	BCP	4.7	4.6	4.7	4.6	4.2
ALP	U/L	IFCC	62	61	4	4	47
ChE	U/L	IFCC	261	257	182	256	230
Fe	mg/dL	Nitroso-PSAP	73	72	-8	-9	65
UIBC	mg/dL	Nitroso-PSAP	233	236	876	882	213
Ca	mg/dL	OCPC	9.6	9.6	-4	-4	8.3
Na	mmol/L	ISE	139	141	197	137	158
K	mmol/L	ISE	4.9	4.7	26	31.7	4.1
Cl	mmol/L	ISE	103	104	102	102	88

TP, total protein; ALB, albumin; ALP, alkaline phosphatase; ChE, choline esterase; Fe, iron; UIBC, unsaturated iron-biding capacity; Ca, calcium; Na, sodium; K, potassium; Cl, chloride

Contributed by:

Dr. Ryunosuke Ohkawa, PhD

Professor, Clinical Analysis and Molecular Biology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University. Member, Communication & Publications Committee

Quiz-Answer Section!!

Answer for question

Tube B: lithium heparin, Tube C: sodium fluoride plus EDTA-2K, Tube D: EDTA-2K, Tube E: sodium citrate

Laboratory rooms sometimes receive blood tubes obtained through incorrect procedures including anticoagulant contaminations. Serious problems could occur if laboratory scientists report the measured values without noticing the error. To avoid reporting incorrect data, laboratory scientists must be able to guess which anticoagulant was used and should know how it affects each analyte value.

Type B:

The test tube with lithium heparin is also commonly used for clinical chemistry testing. Values of most test items are not affected by lithium heparin. However, unlike serum, fibrinogen is included in the plasma containing lithium heparin, resulting in a higher total protein level than in serum.

Type C:

Sodium fluoride is used for blood glucose testing to suppress the glycolysis system by inhibiting enolase activity. It also suppresses choline esterase activity, resulting in falsely low values. Of course, the sodium fluoride contamination increases sodium levels in the plasma. Some test tubes for blood glucose also contain EDTA-2K to allow for simultaneous HbA1c testing. EDTA-2K has an anticoagulant effect by chelating calcium ions, which are essential for coagulation. Since EDTA-2K chelates also other dipole ions like magnesium, iron, and zinc to reduce their levels, it cannot be used for such ion tests. The principle of UIBC testing is based on ion binding by transferrin, and its level is evaluated by detecting a decrease in ion levels. When EDTA-2K chelates iron ions, it produces a falsely high UIBC value. Alkaline phosphatase is an enzyme with zinc in its active site. Therefore, chelation of zinc by EDTA-2K induces alkaline phosphatase deactivation. Serum potassium levels also show high levels due to the addition of EDTA-2K (potassium salt).

Tube D:

Similar changes are observed in plasma with EDTA-2K alone, except for the low choline esterase activity and high sodium level caused by sodium fluoride.

Tube E:

Sodium citrate is a liquid anticoagulant used for coagulation tests such as PT, APTT, and so on. For coagulation tests, sodium citrate is mixed with blood in a 1:9 ratio by volume, so all plasma components are diluted by 10%. Since this liquid contains sodium, only the sodium level is increased.