College of Chemical Pathologists of Sri Lanka

CCPSL NEWSLETTER

2024/2025

Issue 06

COVER STORY

9th Annual Academic Sessions (AAS) 2024
College of Chemical Pathologists of Sri Lanka
NAVIGATING CHALLENGES: QUALITY AT THE FOREFRONT

IN THIS ISSUE

Editors

Dr Dilinika Perera

Dr Maduri Vidanapathirana

Message from the President (2024/2025)

Dr. Thushara Hewageegana
MBBS, Dip Path, MD (Chemical Pathology)
Consultant Chemical Pathologist
TH Anuradhapura
Sri Lanka

Dear Esteemed Members of the College of Chemical Pathologists of Sri Lanka (CCPSL),

I express my gratitude to the two editors of the College of Chemical Pathologists of Sri Lanka (CCPSL) for bringing the 6th issue of the newsletter of the college. Our newsletter provides a solid platform for members to showcase interesting cases, research findings, share their knowledge on current events, and exhibit their artistic skills. I encourage every CCPSL member to participate in the common endeavor of disseminating knowledge by writing and reading. Without a doubt, the future of Chemical Pathology in Sri Lanka and elsewhere will be shaped by our combined efforts.
I appreciate your steadfast dedication and help.

With warm regards,
Dr. HTN Hewageegana
President, College of Chemical Pathologists of Sri Lanka

Email: colchempath@gmail.com Tel: +94 (0) 76 704 4871 Website: ccpsrilanka.com

CCPSL NEWS

Induction of the 9th President of CCPSL and Inauguration Ceremony of Annual Academic Sessions of CCPSL 2024

The induction of the 9th President of the College of Chemical Pathologists of Sri Lanka (CCPSL) and the inauguration of the 9th Annual Academic Sessions, 2024, took place on the 12th and 13th of July at the Galadari Hotel in Colombo.

The inauguration ceremony was a great success, witnessed by a large number of participants. The chief guest for the occasion was Dr. Palitha Gunarathna Mahipala, Secretary of the Ministry of Health.

Dr Thushara Hewageegana was inducted as the 9th President of CCPSL by the immediate Past President, Dr. Dulani Jayawardana. In his presidential address, Dr Hewageegana highlighted the role of a Chemical Pathologist and the services provided in managing patients.

Dr Mala Nandanee Tudawe, Consultant Haematologist, was awarded the CCPSL fellowship in recognition of her exceptional contributions to the field of Pathology and her dedicated service as a healthcare professional, distinguished academic, and exemplary teacher.

Mr Lankananda Baduraliyage, an experienced Senior Medical Laboratory Technologist currently working at Base Hospital Homagama, was felicitated for his remarkable achievements and valuable contributions to the field of Medical Laboratory Technology.

The prestigious CCPSL oration for the third time titled Dyslipidaemia: Current Perspectives and Implications in Clinical Practice" was delivered by Chandrika Meegama, Consultant Chemical Pathologist.

The inauguration concluded with a musical event and a grand reception.

Email: colchempath@gmail.com Tel: +94 (0) 76 704 4871 Website: ccpsrilanka.com

CCPSL NEWS

9th Annual Academic Sessions of CCPSL

The 9th Annual Academic Sessions of the College of Chemical Pathologists of Sri Lanka (CCPSL) were successfully concluded at the Galadari Hotel in Colombo on the 12th and 13th of July, 2024. The event, held under the theme “Navigating Challenges: Quality at the Forefront,” provided two days of new knowledge and insights.

The scientific program featured two parallel tracks: an academic program and a medical laboratory science (MLS) program. The academic program included six plenaries and six symposia covering a wide range of important topics in Chemical Pathology. A historic first for the event was the inclusion of a debate on "Total Lab Automation is the Way Forward in Sri Lanka," which was a highlight. Additionally, a useful breakfast symposium was held on the second day.

Forty-one resource persons, including 12 overseas speakers, contributed to the sessions, sharing their expertise on topics related to renal, metabolic, paediatric, cardiac, bone and calcium, and laboratory management in the symposia.

The event also served as an excellent platform for Chemical Pathology trainees and researchers to present their work. Out of 67 submitted abstracts, 12 were selected for oral presentations, while the remainder were displayed as e-posters. The oral presentation competition, judged by a distinguished panel, was conducted on a pre-scheduled date prior to the main program. The competition aimed to foster research interest and presentation skills among Chemical Pathology and MLS trainees. Winners of the oral presentation and e-poster competitions were announced at the closing ceremony.

The 2024 AAS-CCPSL Clinical Lab Expo ran concurrently with the sessions, open to all attendees and non-registered laboratory professionals interested in the latest diagnostic technologies and developments in laboratory medicine. It provided an opportunity for attendees to interact with exhibitors and find solutions to their laboratory-related needs.

Email: colchempath@gmail.com Tel: +94 (0) 76 704 4871 Website: ccpsrilanka.com

Winners of the awards - 9th Annual Academic Sessions of CCPSL

Oral Presentations (Research and Audits Category)

First place

Evaluation of Efficacy of Sampson Equation for LDL-C; Single Centered Study at a Tertiary Care Hospital in Sri Lanka

Galmangodage NE

Department of Chemical Pathology, National Hospital of Sri Lanka

ne.galmangodage@gmail.com

Second place

Insight into Adrenal Insufficiency: Predicting the Outcome of Short Synacthen Test Based on Baseline Cortisol Levels: Single Centered Retrospective Cohort Study at a Tertiary Care Hospital in Sri Lanka

Premadasa MGTW

Department of Chemical Pathology, National Hospital, Kandy, Sri Lanka

thiliniwathsala110@gmail.com

Third place

Enhancing the Specificity of 17-Hydroxyprogesterone Cut-off Value for Cosyntropin Stimulation Testing. A Retrospective Study of Sri Lankan Population.

Panapitiya NP

Department of Biochemistry, Medical Research Institute, Colombo, Sri Lanka

neisali@yahoo.com

Oral Presentations (Case Report Category)

First place

Reninoma- Rare Cause of Young Hypertension

Arooran T

Department of Chemical Pathology, Lady Ridgeway Hospital for Children, Colombo

thayaniarooran@gmail.com

Second place

A Diagnostic Dilemma of TSHoma in a Clinically Euthyroid Patient: A Case Report

Liyanagunawardana JE

Department of Chemical Pathology, National Hospital of Sri Lanka

ewmi.janee26@gmail.com

Third place

Glycerol Kinase Deficiency in a Child with Muscular Dystrophy - Importance of Laboratory Investigations in the Evaluation of Suspected Contiguous Gene Deletion Syndrome

Rajalingam M

Department of Chemical Pathology, Lady Ridgeway Hospital for Children, Colombo 08, Sri Lanka

nrmaathu@gmail.com

E-Poster Presentations (Research and Audits Category)

First place

Relationship between the Blood Pressure and Serum Uric Acid Levels in Pregnant Women

Madhurahini R

Department of Biochemistry, Faculty of Medicine, University of Jaffna, Sri Lanka

madu110398@gmail.com

Second place

Multiple Regression Model for the Prediction of Postoperative Hypocalcaemia by Using Preoperative Serum Magnesium (Mg) and Intraoperative Plasma Intact Parathyroid Hormone (iPTH) Levels among Patients Undergoing Total Thyroidectomy

Pathirana VPATV

Department of Chemical Pathology, Teaching Hospital Badulla, Sri Lanka

thathsarani1609@gmail.com

Third place

The Effect of "Teepol" Residues on the Estimation of Serum Electrolytes, Protein and Cholesterol in Sample Collection Tubes: An Interference Study

Jayasekara D

Department of Chemical Pathology, Colombo North Teaching Hospital, Ragama, Sri Lanka,

dtjdilini@gmail.com

Third place

Saliva as an Alternative to Blood for the Assessment of Kidney Function in Chronic Kidney Disease Patients; An Analytical Cross-Sectional Study at Teaching Hospital Karapitiya, Sri Lanka

Dilrangi VLT

Department of Medical Laboratory Science, Faculty of Allied Health Sciences, University of Ruhuna

tharakaadilrangi@gmail.com

E-Poster Presentations (Case Report Category)

First place

Hypertension, Hyperkalaemia and Metabolic Acidosis and Low Serum Renin Activity: A Case Report on Pseudohypoaldosteronism Type 2 in a Six-Year-Old Child

Fernando K

Professorial Paediatric Unit,Lady Ridgeway Hospital for Children,Colombo,Sri Lanka
Department of Biochemistry and Clinical Chemistry,Faculty of Medicine,University of Kelaniya,Sri Lanka

kavindyam@kln.ac.lk/
kavindyamjn14@gmail.com

Second place

Case Report of Three Siblings with Familial Chylomicronaemia Syndrome Due to a Homozygous Lipoprotein Lipase Variant, Arg270Gly

Yoganathan H

Department of Chemical Pathology,Teaching Hospital Batticaloa,Sri Lanka

hemiyoga@gmail.com

Third place

Vomiting and Ketosis in a Child Leading to a Diagnosis of a Rare Metabolic Disorder; A Case Report

Liyanagunawardana JE

Department of Chemical Pathology, Lady Ridgeway Hospital for Children, Colombo

ewmi.janee26@gmail.com

Measuring lipids; the way forward in Sri Lanka

Dr Gaya Katulanda
Consultant Chemical Pathologist
National Hospital of Sri Lanka, Colombo

Dr Dilini Jayasekara
Senior Registrar in Chemical Pathology
National Hospital of Sri Lanka, Colombo

Dr Pavithra Samarakoon
Senior Registrar in Chemical Pathology
National Hospital of Sri Lanka, Colombo

Justification

Measuring lipids in blood plays a major role in atherosclerotic cardiovascular disease (ASCVD) risk assessment and in monitoring of the success of the lipid lowering therapy. Still ASCVD remains a leading cause of morbidity and mortality globally and locally. Many professional organizations, individuals and multi-billion companies work tirelessly to find the best possible means of assessing ASCVD risk. Blood lipids is one precisely measurable parameter in the risk assessment. The measurement procedures, interpretations, and estimation of risk are evolving day by day. Moreover, new lipid parameters are emerging. This article describes lipid measurements, recent changes in interpretation and emerging lipid parameters with a view to introduce into routine practice in Sri Lanka.

South Asian individuals have at least a 2-fold increased risk of ASCVD and diabetes[1] compared to world population. The prevalence of diabetes among adults is alarmingly high at 23% in Sri Lanka [2]. Furthermore, every 2 out of 3 Sri Lankan adults are found to have some sort of dyslipidaemia according to several studies [3, 4]. The Global Burden of Disease (GBD) indicates that worldwide 4.4 million deaths were attributed to elevated low-density lipoprotein cholesterol (LDLC) in 2019, which accounted for 12.6% of all risk-related deaths [5].

New equations to estimate LDLC

The importance of accurate measurement of LDLC is increasingly recognized as lipid lowering treatment is more intensified and stringent control has become a prime concern in the prevention of ASCVD. LDLC is an estimated parameter using total cholesterol (TC), high density lipoprotein cholesterol (HDLC) and triglycerides (TG). The Friedewald equation, which was developed in 1972 is commonly used for LDLC estimation. The equation had been validated in a population with higher LDLC levels compared to present day treated populations at high risk of ASCVD and only 35 subjects out of the total study population of 448 had LDLC levels less than 100 mg/dL [6]. Continuing studies are showing that equation underestimates LDLC at lower LDLC levels [7]. It is of concern that falsely low LDLC values may lead to postponement of initiation of therapy or delayed intensification of therapy. However, it was recognized from the outset that the equation underestimated LDLC at higher TG levels and was not used when TG is more than 400 mg/dL. As a result, number of laboratories across the world has started using more expensive direct assays to measure LDLC when TG is more than 400 mg/dL.

New equations surfaced to combat the short comings in the Friedewald equation. The Martin Hopkins formula, developed from 13.5 million sample data and published in 2013 was found to be more accurate at LDLC levels less than 70 mg/dL. However, it showed limitations at higher TG levels and still couldn't be used confidently when TG is more than 400 mg/dL.The equation had a variable factor for TG concentration and was more complicated during application.

The Sampson-NIH equation published in 2020 was better than both formulae. It showed the advantages of being more accurate when LDLC was low (less than 70 mg/dL), and TG was high up to a level of 800 mg/dL [8]. A cohort study based on Chinese population has stated Sampson-NIH equation is more accurate compared to Friedewald formula in relation to acute coronary syndrome [9].Globally Sampson-NIH equation is progressively recommended to be used for calculating LDLC and is recognized by the Association for Diagnostics & Laboratory Medicine (ADLM) too [10]. Moreover, LDLC by Sampson-NIH equation is highly accurate as it is derived in comparison with the gold standard ß-quantification reference method for LDLC. The Sampson-NIH equation avoids the limitation of discrete factor approach, creating a smooth factor line enabling estimation of LDLC in a continuous, predictable manner. Also, it is simpler to apply in Laboratory Information Systems, compared to Martin equation.

A study conducted at the National Hospital; Sri Lanka (NHSL) that included 287 patient samples revealed that the LDLC levels from the Sampson-NIH formulae have a good correlation with direct LDLC measurement which was used as the reference method for LDLC. Moreover, the study showed a clear negative bias in Freidewald derived LDLC values, especially at concentrations below 100 mg/dL in comparison to LDLC by both Sampson-NIH and Martin equations [11]. Based on the study findings and according to the practice in the UK and other developed countries, we started using Sampson-NIH for LDLC estimation since September 2024 at NHSL. As LDLC is calculated up to TG levels of 800 mg/dL the necessity to perform direct LDLC using expensive assays was withheld. When TG is above 800 mg/dL the primary treatment target is to bring down TG, where LDLC estimation can be postponed [12].

Hands on risk indicator; Non-HDLC

Non-high-density lipoprotein cholesterol (non-HDLC) has gained assurance as a key risk indicator for ASCVD and a therapeutic target since 2002 [13]. Non-HDLC is a measure of cholesterol content in all atherogenic particles (low density lipoprotein, very low-density lipoprotein and intermediate density lipoprotein particles and chylomicrons) that leads to plaque formation and atherosclerosis. It is a more accurate measure of total atherogenic load [14]. The calculation is simple by subtracting HDLC from TC, and interpretation is equally simple. Moreover, it can be estimated in a non-fasting sample.

New lipid parameters; apolipoprotein B and lipoprotein(a)

There are two emerging ASCVD risk indicators incorporated in international guidelines, yet the importance and clinical significance are to be explored in Sri Lanka. Lipoprotein(a) (Lp(a)) is one such risk predictor, which is a lipoprotein particle, structurally similar to low density lipoprotein particles, inclusive of an additional apolipoprotein named apo(a). It has atherogenic,thrombogenic and pro-inflammatory effects leading to ASCVD. It is identified as an independent risk factor for ASCVD by many studies [15, 16]. When Lp(a) level is greater than 180 mg/dL, the risk of ASCVD is very high and similar to heterozygous familial hypercholesterolaemia [17]. Lp(a) levels are genetically determined, and South Asians are known to have higher Lp(a) levels than Caucasians [18]. The 2019 ESC/EAS dyslipidaemia guidelines recommend Lp(a) measurement at least once in lifetime in every adult and repeat testing under specific indications [19]. It is used when there is a family history of premature heart disease and for reclassification of risk level in people at borderline between moderate and high-risk [19].

The other emerging principal risk indicator is apolipoprotein B (apoB) which is an apoprotein constituent in atherogenic lipoprotein particles. Each atherogenic lipoprotein particle contains a single apoB molecule. Hence apoB concentration is a direct measure of number of all atherogenic lipoprotein particles. The trapping of apoB containing particles within the arterial wall and the injury to arterial wall ismore when the number apoB particles within the lumen is higher [20]. ApoB analysisis considered a better target for ASCVD risk assessment and treatment monitoring than LDLC and non-HDLC [21]. The concentration of LDLC and non-HDLC depends on the amount of cholesterol carried in apoB containing particles. The extent of injury depends on the amount of cholesterol as well as number of apoB containing particles. ApoB can be used as an alternative to LDLC, if available, as the primary measurement for screening, diagnosis, and management, and may be preferred over non-HDL-C in people with high TG levels, DM, obesity, or very low LDL-C level [19]. Moreover, the analytical performances of apoB assay methods based on immunology are superior to the measurement or calculation of LDL-C and non-HDL-C [22] . There are standardized, automated, accurate, and inexpensive methods available for both apoB and Lp(a) measurements on common chemistry platforms. Both measurements can be done on non-fasting blood samples.

Non-fasting lipid profile; time to change

In Sri Lanka the practice to date is to measure lipids in a fasting sample where patient is advised to fast for 10-12 hours overnight. Requirement of 10-12 hours fasting for lipid measurement is inconvenient for the patients and delays the findings related to lipid metabolism to the clinician, required for clinical decision making. Accordingly, many studies have been conducted globally to investigate the applicability of non-fasting lipid profiles instead of fasting lipid profiles. Journal of American College of Cardiology explains that non-fasting sample represents body's usual atherogenic lipoproteins more than by a fasting sample [23]. It is studied and show cased that non-fasting lipid profiles have maximum mean change of +26 mg/dL for TG, -8 mg/dL for TC, -8 mg/dL for LDLC, +8 mg/dL for remnant cholesterol, and -8 mg/dL for non–HDLC whereas Lp(a), ApoB, and HDLC are largely unaffected compared to fasting lipid profiles [23]. It is shown that the observed difference between

non-fasting and fasting lipid profiles are independent of statin treatment [24] and presence of diabetes mellitus, a common disease altering lipid metabolism [25]. Also, non-fasting lipids are shown to be directly related to CVD risk [26,27]. ADLM also gives supportive evidence for using non-fasting lipid profiles and further recommends to repeat a fasting lipid profile if the non-fasting TG >400 mg/dL[28, 29]. We can enjoy the advantage of using the Sampson-NIH formula which calculates LDLC up to a TG level of 800 mg/dL, for non-fasting lipid profiles when TG is expected to be higher.

However, the dietary pattern and genetic background is not identical for the Sri Lankans when compared with global community and therefore, more evidence is needed in Sri Lankan context regarding correlation between fasting and non-fasting lipid profiles. A study conducted among 84 health care workers in Batticaloa has revealed statistically significant differences for TC, HDLC, LDLC, non-HDLC between fasting and non-fasting samples [30]. More evidence is needed regarding the applicability of non-fasting lipid profiles in the Sri Lankan context as clinicians seem to have a reluctance in changing the practice, and a study to evaluate such is on its way.

Is reporting of lipids up to date?

Let us explore how measuring lipids evolved in Sri Lanka. Being a country with high prevalence of dyslipidaemia, diabetes and metabolic syndrome and despite spending considerably on lipid lowering medications as well as curative procedures, the availability of proper risk assessment markers is a mandatory need. In the early two thousand, TC was the only freely available ASCVD risk marker in most of the state hospitals. Soon lipid profiles with calculated LDLC became abundantly available. Today LDLC is the commonly used risk indicator in treated and untreated populations while the use of non-HDLC is on the rise. It is time to adopt calculating LDLC by Sampson formula throughout the country as a significant percentage of individuals on treatment have LDLC levels below 100 mg/dL. Another drawback is the lack of uniformity in lipid profile reporting. Different reference ranges or decision limits are indicated on the lipid profile reports by different laboratories both private and state. This has been a worldwide problem, and different groups have made consensus statements to achieve uniformity in lipid profile reporting. It is suggested to include desirable lipid values in adults in relation to ASCVD risk and prevention, according to the European Societies of Arteriosclerosis and Laboratory for laboratories in Spain, as a published consensus document [31].It is recommended for Australian pathology laboratories to include a statement of likely lipoprotein abnormality with possible causes based on patient's clinical data and to avoid such comments when an experienced clinician has requested the test and when the patient is already diagnosed and treated for a lipid disorder [32]. According to the ADLM recommendations, desirable concentrations need to be displayed on the report, and they are 50th percentile for TC, HDLC, LDLC, TG, Non-HDLC, ApoB in adults. In children these limits are set to 75th percentile for TC, Non-HDLC, TG and 25th percentile for HDLC and 90th percentile for LDLC, apoB. Inclusion of fasting status during sample collection in the report is also recommended [29].It is essential to adhere to uniform reporting system for lipid profiles in Sri Lanka based on this evidence to resolve the chaos in lipid profile interpretation. A consensus group of experts comprising of chemical pathologists, physicians, cardiologists and epidemiologists shall get together to decide on a proper reporting system. In addition,apoB and Lp(a) shall be introduced into risk assessment and further studies shall be carried out to check the outcome.

In conclusion, Sri Lanka needs evidence-based shift in practices from fasting to non-fasting lipid profiles, application of Sampson-NIH equation for LDLC calculation, introduction of Lp(a) and apoB measurements and harmonization of rational reporting format for lipid profiles across the island.

References

1. Quantifying and Understanding the Higher Risk of ASCVD Among South Asians - American College of Cardiology [Internet]. [cited 2024 Sep 25]. Available from: https://www.acc.org/Latest-in-Cardiology/Articles/2021/09/13/14/42/Quantifying-and-Understanding-the-Higher-Risk-of-ASCVD-Among-South-Asians
2. Prevalence of diabetes and pre-diabetes in Sri Lanka: a new global hotspot–estimates from the Sri Lanka Health and Ageing Survey 2018/2019 | BMJ Open Diabetes Research & Care [Internet]. [cited 2024 Sep 25]. Available from: https://drc.bmj.com/content/11/1/e003160
3. Katulanda P, Dissanayake HA, De Silva SDN, Katulanda GW, Liyanage IK, Constantine GR, et al. Prevalence, patterns, and associations of dyslipidaemia among Sri Lankan adults-Sri Lanka Diabetes
and Cardiovascular Study in 2005-2006. J Clin Lipidol. 2018;12(2):447–54.
4. Nandasena HMRKG, Tennakoon TMSUB, Ralapanawa DMPUK. Prevalence and determinants of dyslipidemia among adults in the community: A cross-sectional study in a selected province, Sri Lanka. Clin Epidemiol Glob Health. 2023 Nov 1;24:101442.
5. Zheng J, Wang J, Zhang Y, Xia J, Guo H, Hu H, et al. The Global Burden of Diseases attributed to high low-density lipoprotein cholesterol from 1990 to 2019. Front Public Health [Internet]. 2022 Aug 16 [cited 2024 Sep 19];10. Available from: https://www.frontiersin.org/journals/public-health/articles/10.3389/fpubh.2022.891929/full
6. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem. 1972 Jun;18(6):499–502.
7. Wang I, Rahman MH, Hou S, Lin HW. Assessing the Practical Differences in LDL-C Estimates Calculated by Friedewald, Martin/Hopkins, or NIH Equation 2: An Observation Cross-Sectional Study. J Lipid Atheroscler. 2023 Sep;12(3):252–66.
8. Sampson M, Ling C, Sun Q, Harb R, Ashmaig M, Warnick R, et al. A New Equation for Calculation of Low-Density Lipoprotein Cholesterol in Patients With Normolipidemia and/or Hypertriglyceridemia. JAMA Cardiol. 2020 May;5(5):1–9.
9. Evaluation of Sampson equation for LDL-C in acute coronary syndrome patients: a Chinese population-based cohort study - PMC [Internet]. [cited 2024 Sep 22]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9016968/
10. Sampson M, Wolska A, Meeusen JW, Otvos J, Remaley AT. The Sampson-NIH Equation Is the Preferred Calculation Method for LDL-C. Clin Chem. 2024 Feb 1;70(2):399–402.
11. Balasooriya BMCM, Basnayake BMTK, Galmangodage NE, Liyanagunawardana JE, Siddiqa OMO, Manathunga SS, Katulanda GW. Evaluation of Efficacy of Sampson Equation for LDL-C; Single Centered Study at a Tertiary Care Hospital in Sri Lanka. Oral Presentation presented at: 9th Annual Academic Sessions, College of Chemical Pathologists Sri Lanka; 2024; Abstract Book.

12. American College of Cardiology [Internet]. [cited 2024 Sep 26]. Hypertriglyceridemia Management According to the 2018 AHA/ACC Guideline. Available from: https://www.acc.org/latest-in-cardiology/articles/2019/01/11/07/39/http%3a%2f%2fwww.acc.org%2flatest-in-cardiology%2farticles%2f2019%2f01%2f11%2f07%2f39%2fhypertriglyceridemia-management-according-to-the-2018-aha-acc-guideline
13. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation. 2002 Dec 17;106(25):3143–421.
14. Virani SS. Non-HDL Cholesterol as a Metric of Good Quality of Care. Tex Heart Inst J. 2011;38(2):160–2.
15. Berg K, Dahlén G, Christophersen B, Cook T, Kjekshus J, Pedersen T. Lp(a) lipoprotein level predicts survival and major coronary events in the Scandinavian Simvastatin Survival Study. Clin Genet. 1997 Nov;52(5):254–61.
16. Seman LJ, DeLuca C, Jenner JL, Cupples LA, McNamara JR, Wilson PW, et al. Lipoprotein(a)-cholesterol and coronary heart disease in the Framingham Heart Study. Clin Chem. 1999 Jul;45(7):1039–46.
17. Burgess S, Ference BA, Staley JR, Freitag DF, Mason AM, Nielsen SF, et al. Association of LPA Variants With Risk of Coronary Disease and the Implications for Lipoprotein(a)-Lowering Therapies: A Mendelian Randomization Analysis. JAMA Cardiol. 2018 Jul 1;3(7):619–27.
18. D'Amore M, O'Brien R. Elevated Lipoprotein (a) in Asian Populations and its Implications for Cardiovascular Disease. Heart Lung Circ. 2023 Jul 1;32:S387.
19. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk | European Heart Journal | Oxford Academic [Internet]. [cited 2024 Sep 22]. Available from: https://academic.oup.com/eurheartj/article/41/1/111/5556353
20. Sniderman AD, Thanassoulis G, Glavinovic T, Navar AM, Pencina M, Catapano A, et al. Apolipoprotein B Particles and Cardiovascular Disease: A Narrative Review. JAMA Cardiol. 2019 Dec 1;4(12):1287–95.
21. Contois JH, McConnell JP, Sethi AA, Csako G, Devaraj S, Hoefner DM, et al. Apolipoprotein B and cardiovascular disease risk: position statement from the AACC Lipoproteins and Vascular Diseases Division Working Group on Best Practices. Clin Chem. 2009 Mar;55(3):407–19.
22. Quantifying Atherogenic Lipoproteins: Current and Future Challenges in the Era of Personalized Medicine and Very Low Concentrations of LDL Cholesterol. A Consensus Statement from EAS and EFLM - PubMed [Internet]. [cited 2024 Sep 25]. Available from: https://pubmed.ncbi.nlm.nih.gov/29760220/
23. Nordestgaard BG. A Test in Context: Lipid Profile, Fasting Versus Nonfasting. J Am Coll Cardiol. 2017 Sep 26;70(13):1637–46.
24. Liu MM, Peng J, Cao YX, Guo YL, Wu NQ, Zhu CG, et al. The difference between fasting and non-fasting lipid measurements is not related to statin treatment. Ann Transl Med. 2021 Mar;9(5):386–386.
25. Langsted A, Nordestgaard BG. Nonfasting lipids, lipoproteins, and apolipoproteins in individuals with and without diabetes: 58 434 individuals from the Copenhagen General Population Study. Clin Chem. 2011 Mar;57(3):482–9.

26.Langsted A, Nordestgaard BG. Nonfasting versus fasting lipid profile for cardiovascular risk prediction. Pathology (Phila). 2019 Feb 1;51(2):131–41.
27.Mora S, Rifai N, Buring JE, Ridker PM. Fasting compared with nonfasting lipids and apolipoproteins for predicting incident cardiovascular events. Circulation. 2008 Sep 2;118(10):993–1001.
28.Langsted A, Nordestgaard BG. Worldwide Increasing Use of Nonfasting Rather Than Fasting Lipid Profiles. Clin Chem. 2024 Jul 1;70(7):911–33.
29.Cao J, Donato L, El-Khoury JM, Goldberg A, Meeusen JW, Remaley AT. ADLM Guidance Document on the Measurement and Reporting of Lipids and Lipoproteins. J Appl Lab Med. 2024 Sep 3;9(5):1040–56.
30.Umakanth M, Ibrahim M. Fasting and Non-Fasting Lipid Profile among Health Care Workers at Teaching Hospital Batticaloa SriLanka. J Biosci Med. 2018 Jul 5;6(7):15–22.
31.Consensus document for lipid profile determination and reporting in Spanish clinical laboratories. What parameters should a basic lipid profile include? [Internet]. [cited 2024 Sep 22]. Available from: http://www.elsevier.es/en-revista-neurology-perspectives-17-avance-resumen-consensus-document-for-lipid-profile-S2667049623000182
32.Appleton CA, Caldwell G, McNeil A, Meerkin M, Sikaris K, Sullivan DR, et al. Recommendations for Lipid Testing and Reporting by Australian Pathology Laboratories. Clin Biochem Rev. 2007 May;28(2):32–45.

Serum Free Light-Chain Assay, for the Diagnosis and Monitoring of Plasma Cell Disorders

Dr Rajitha Samarasinghe
Consultant Chemical Pathologist
National Cancer Institute, Sri Lanka

Introduction

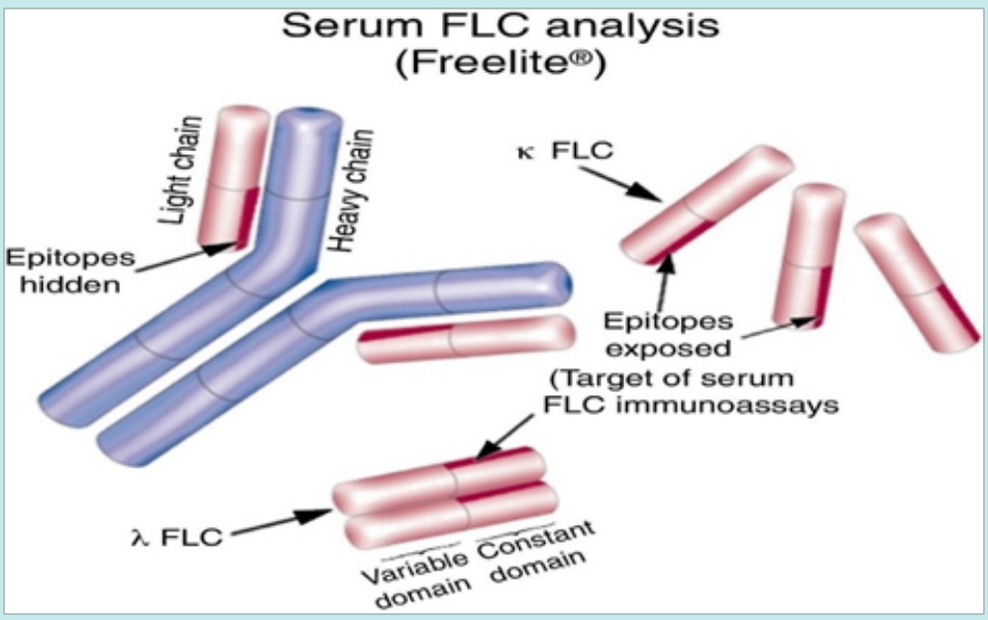
Plasma cell disorders are a diverse group of disorders of unknown etiology characterized by

- Disproportionate proliferation of single clone of beta cells
- Presence of a structurally and electrophoretically homogenous (monoclonal) immunoglobulin or polypeptide subunits in serum, urine or both.

The disorders could range from indolent disorders such as monoclonal gammopathy of undetermined significance (MGUS) to severe life-threatening diseases such as multiple myeloma (MM) or amyloid light-chain amyloidosis (AL). The mainstay of diagnosis and monitoring of these disorders is the assessment of an abnormal monoclonal immunoglobulin (M band) in serum and/or urine, by electrophoresis and immunofixation. But the value of above investigations is questionable in conditions like nonsecretory and oligosecretory myeloma where no direct correspondence exists between the tumour burden and the amount of M proteins.

In the early 2000s, an assay was developed aimed at evaluating an epitope 'hidden' in intact immunoglobulin and 'visible' in free light chains (FLC) and was made available for and subsequently tested in different plasma cell disorders, such as oligosecretory and nonsecretory MM, light chain myeloma and amyloidosis and found to be useful in the diagnosis and monitoring of these disorders.

Serum free light chains (sFLC)



Email: colchempath@gmail.com Tel: +94 (0) 76 704 4871 Website: ccpsrilanka.com

Light chains are kappa (κ) and lambda (λ) bound to heavy chains by a disulfide bridge. Any given antibody molecule has a light chain but never both.

Plasma cells produce one of five heavy chain types together with κ or λ molecules. There is approximately 40% excess FLC production over heavy chain synthesis to allow proper conformation of the intact immunoglobulin molecules.

There are twice as many κ producing plasma cells as λ, and κ chains are monomeric whereas λ chains are dimeric.

FLCs are rapidly cleared and metabolized by the kidneys depending upon their molecular size. The monomeric κ FLCs, are cleared rapidly than the dimeric λ FLCs, although κ production rates are twice that of λ, its faster removal ensures that the actual serum concentrations are approximately 50% lower.

Once filtered FLCs are completely reabsorbed in the proximal convoluted tubules (PCT). Under normal conditions non pass beyond PCT.

Uses of sFLCs measurements

Intact immunoglobulin multiple myeloma (HCMM)

In the diagnosis–

sFLCs ratios are abnormal in 95% of patients at disease presentation, therefore sFLC is essential in the diagnostic workup. (Ideally both SPE and sFLC should be performed at the time of the diagnosis) SFLC shows no correlation with intact immunoglobulin concentrations but correlates better with bone marrow data.

In follow up and monitoring-

sFLC has a shorter half-life than intact immunoglobulins, can detect lack of response to therapy and disease relapse earlier than SPE.

In smouldering multiple myeloma (SMM)

A firm conclusion is not yet drawn in the use of sFLC in SMM, but it appears that in the spectrum of disease development from MGUS, through asymptomatic to symptomatic MM, excess monoclonal sFLC production becomes progressively more probable.

Non secretory multiple myeloma (NSMM)

NSMM accounts for about 1- 5 % of all MM patients.
The disease is characterized by the absence of monoclonal immunoglobulins in serum and urine

using electrophoresis, as most of these patients have tumour cells that produce, but do not secrete monoclonal immunoglobulins into the blood.

Nevertheless, monoclonal proteins can usually be demonstrated in the bone marrow cells by immunohistochemical staining.

10-15% of NSMM are true 'non-producers'. In these patients the tumour plasma cells contain no detectable immunoglobulins.

With the development of sensitive assays, measurement of sFLC levels has become the maintain stay of disease monitoring for NSMM, instead of frequent invasive marrow examinations.

The addition of sFLC evaluation to the diagnostic work up has demonstrated that an average 70% of cases produce a monoclonal LC, thus rendering the sFLC assay useful in monitoring disease response and relapse.

Light chain multiple myeloma (LCMM)

Approximately 50% of patients with LCMM will demonstrate a monoclonal band in SPE. Some of the remainder will demonstrate a hypogammaglobulinaemia.

IFIX will demonstrate a monoclonal band and finally a urine electrophoresis is required to identify the monoclonal FLCs.

Some studies have shown that since immunoassays for sFLC are more sensitive than electrophoresis tests they could eliminate the need for urine testing.

Serum free light chains for assessing residual disease

Absence of monoclonal proteins after high-dose therapy is a good prognostic indicator.

Some patients considered to be in complete remission by electrophoretic tests might be reclassified as having residual disease by the more sensitive sFLC tests.

Abnormal sFLC levels indicate residual disease and poor survival probability.

The serum levels of FLC respond faster to therapy than immunoglobulins as their half-life is shorter.

In summary – normal SPE/IFIX with abnormal sFLC in a patient with residual disease is a bad prognostic indicator and, normal sFLC with abnormal SPE/IFIX in a patient going into complete remission is a good indicator as due to its short half-life light chains disappear earlier during treatment.

Email: colchempath@gmail.com Tel: +94 (0) 76 704 4871 Website: ccpsrilanka.com

Free light chains and nephrotoxicity

30% of patients with MM have significant renal impairment at disease presentation.

In normal individuals FLCs are rapidly cleared by the kidneys depending on the molecular size, (monomeric κ cleared rapidly and dimeric λ cleared much slowly).

After filtration by the glomeruli, FLCs enter the proximal convoluted tubules (PCT) binds to brush border membranes via a high affinity receptor called cubulins. Binding provokes internalization and subsequent metabolism.

The concentration of FLCs leaving proximal convoluted tubules depends on the amount in glomerular filtrate, competition for binding with other proteins and absorptive capacity of tubular cells.

A reduction in glomerular filtration rate will increase sFLC levels so that more is filtered by the remaining functioning nephrons, and with increasing renal dysfunctions more proteins including albumin will enter PCTs, increasing the competition for the binding proteins.

All above factors will increase the amount of FLCs entering the distal convoluted tubules (DCT). FLCs entering the DCT bind to uromucoid (Tamm-Horsfall protein). Together the two proteins form a waxy cast which are characteristic in acute renal failure found in LCMM. These proteins obstruct tubular fluid flow, leading to basement membrane damage and interstitial damage.

Further rise in sFLCs leads to more filtration by unaffected nephrons causing more to enter PCTs leading to a vicious cycle of accelerating renal damage.

Other malignancies with monoclonal free light chains

- Solitary plasmacytoma of bone

50% of patients will show a small M band in serum/urine. When present it is a useful guide for therapy and follow-up.

Addition of sFLCs will provide a more accurate identification of progression and response to therapy than other markers alone.

- Extramedullary plasmacytoma

Use of sFLCs gives the same benefits as is solitary plasmacytoma.

- Plasma cell leukaemia

No evidence available to suggest the presence of monoclonal sFLCs.

- Waldenstrom's macroglobulinaemia (WM)

SFLCs are frequently abnormal in patients with Waldenstrom's macroglobulinaemia.Their short half-life and large clinical range provide a sensitive marker for treatment response. Also, FLCs do not cryoprecipitate and are not affected by other factors that make IgM measurement difficult.
In WM sFLCs are helpful,

1. As prognostic markers
2. To distinguish WM from IgM MGUS.
3. As an additional criterion for treatment response or disease relapse.

Renal diseases and free light chains

Elevated polyclonal FLCs in serum (associated with normal ratios) results from reduced renal clearance. Reduced clearance of sFLCs results from impaired renal glomerular filtration rate. As GFR falls, sFLC concentration rise and may be 20-30 times normal in end stage renal failure.
With deteriorating renal function κ/λ ratios gradually increase and eventually equal the κ/λ production rates of approximately 1.8:1 in end stage renal failure.

Percentage of accuracy of diagnostic tests at clinical presentation

Protocols	MM	AL Amyloidosis	MGUS
1. SPE alone	90	50	45
2. SPE and IFIX	95	70	80
3. SPE and UPE	95	75	70
4. SPE,UPE,serum and urine IFIX	97	90	80
5. FLC alone	96	95	30-65
6. SPE and FLC	99	98	85
7. SPE, FLC, IFIX	99	99	100

References

1. Bradwell AR. (2010) Serum Free Light Chain Analysis (6thed.), The binding sit.
2. Bidet A, Marit G, Bernard AM. (2008). Clinical value of the blood measurement of the free light chains of immunoglobulins. Ann Biol Clin (Paris),66:427-31.
3. Tate JR, Mollee P, Dimeski G, Carter AC, Gill D. (2007). Analytical performance of serum free light-chain assay during monitoring of patients with monoclonal light chain disease. Clin Chim Acta 2007; 376:30-36.

Biomarkers related to Alzheimer disease

Dr Thathsarani Vithana Pathirana
Consultant Chemical Pathologist
Teaching Hospital Badulla

Introduction

Alois Alzheimer first described the neurodegenerative disease that would bear his name more than 100 years ago, and today the cardinal features of amyloid plaques and neurofibrillary tangles that he described are still required for its pathological diagnosis[1]. Alzheimer's disease (AD) is a progressive neurodegenerative disease most often characterized by initial memory impairment and cognitive decline that can ultimately affect behaviour, speech, visuospatial orientation and the motor system, and it is the most common form of dementia[2]. AD is also characterized by a long asymptomatic preclinical phase, and cognitively normal individuals can also have the disease[3]. While treatments are available that can eliminate some symptoms of the illness, there is no cure or disease-modifying therapy and the disease inevitably progresses in all patients[5].

It is estimated that more than 47 million people in the world are affected by dementia, and as of 2018, the cost of these diseases was expected to surpass $1 trillion annually[6].

Etiology

More common late onset AD (LOAD) is considered sporadic, although genetic risk factors have been identified, most notably apolipoprotein E gene (APOE)[5]. Age, family history in a first degree relative, and APOE4 genotype confer the greatest risks of developing AD[7].

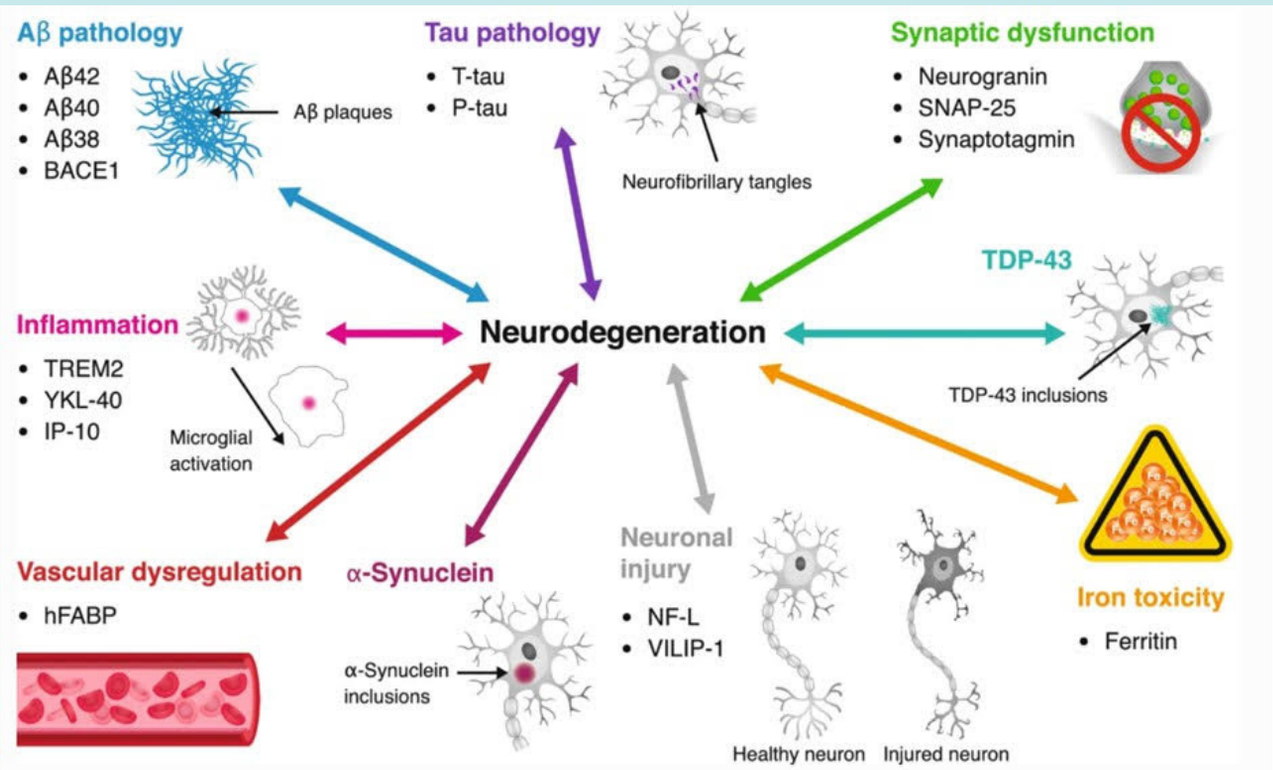
Dominantly inherited familial AD (FAD) can be caused by mutations in amyloid precursor protein (APP), presenilin1 (PSEN1) or PSEN2 genes. These rare familial forms of AD account for less than 1% of the cases.FAD can present as early as age 20, with the average age of onset of 46.2 years[8].

Similarly, most Down's syndrome patients with a partial or full chromosome 21 trisomy, which includes the region on chromosome 21 where APP resides, have Alzheimer type pathology by age 40 with many developing clinical symptoms after 50 years of age and the majority have dementia by age 65[7,9].

Diagnosis

The pathologic diagnosis of AD remains the gold standard for diagnosis. Therefore, clinical AD dementia cannot be definitively diagnosed until post-mortem neuropathologic evaluation.

Biomarkers associated with neurodegeneration



Pathological mechanisms implicated in AD and associated fluid biomarkers. In this figure, the arrows reflect hypothetical relationships, not direct causal links between the pathological mechanisms and neurodegeneration. Only select pathological mechanisms (and associated biomarkers) of AD are represented. *Aβ38* amyloid beta 38, *Aβ40* amyloid beta 40, *Aβ42* amyloid beta 42, *AD* Alzheimer's disease, *BACE1* β-site amyloid precursor protein cleaving enzyme 1, *hFABP* heart-type fatty acid-binding protein, *IP-10* interferon-γ-induced protein 10, *NF-L* neurofilament light, *P-tau* phosphorylated tau, *SNAP-25* synaptosome-associated protein 25, *TDP-43* transactive response DNA-binding protein 43, *TREM2* triggering receptor expressed on myeloid cells 2, *T-tau* total tau, *VILIP-1* visinin-like protein 1

CSF biomarkers

Out of the neurodegenerative markers, Aβ1-42, t-tau, and p-tau are the markers extensively studied as AD biomarkers.

According to the amyloid cascade hypothesis, the initiating event in AD pathogenesis is an imbalance between the production and clearance of amyloid-β1–42 (Aβ42) leading to accumulation of amyloid plaques in the brain that damages the synaptic function and mediates the formation of neurofibrillary tangles. Moreover, Aβ1-42 is the most abundant form of Aβ protein found in amyloid plaques and the reduced concentration of Aβ1-42 in CSF of individuals with AD pathology is presumed to reflect aggregation of Aβ1-42 in brain parenchyma[10]. Aβ-42 is the most fibrillogenic and low levels correlate well with greater plaque load[11].

An increase in CSF t-tau levels likely reflects an index of neurodegeneration and have been shown to correlate with the amount of neurofibrillary tangles in the brain. Importantly, multiple studies have shown that individuals with mild cognitive impairment (MCI) who progressed to AD dementia

Email: colchempath@gmail.com Tel: +94 (0) 76 704 4871 Website: ccpsrilanka.com

have decreased levels of CSF A1-42 together with increased levels of CSF total tau (T-tau) and phosphorylated tau (P-tau)[12,13].

However, it should be recognized that although elevated levels of t-tau reflect an ongoing neurodegenerative process, the localization within different brain circuits can vary widely which is consistent with variance in the symptoms expressed across different neurodegenerative disorders.

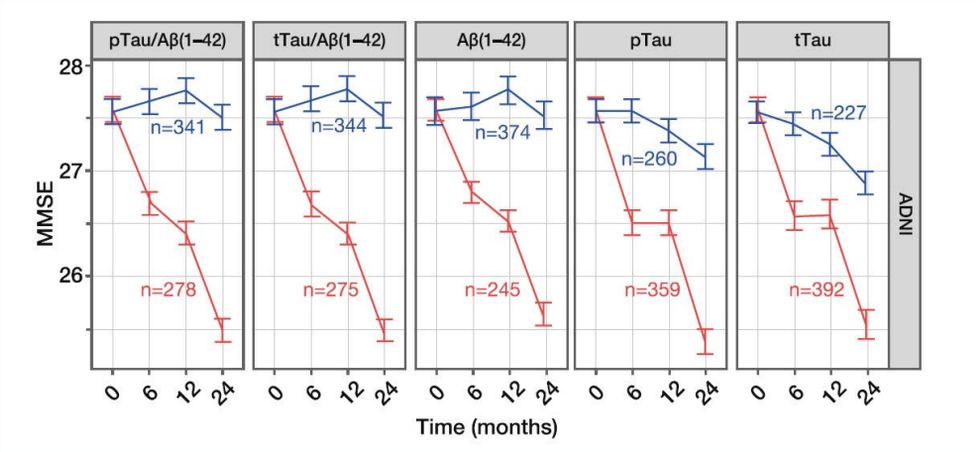
Based on evidence, these CSF biomarkers offer approximately 80-90% sensitivity and specificity for clinically overt AD and valuable prognostic information in patients with amnestic mild cognitive impairment.However, the assessing amyloid and tau burden in living patients are challenging.

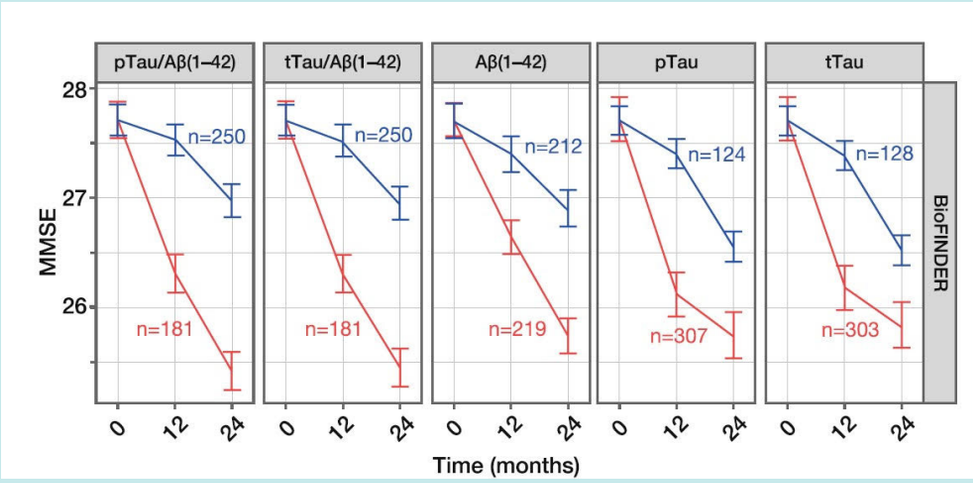
The advantages of CSF biomarkers over imaging techniques include lower cost and the opportunity to detect other pathologies by the same procedure, for example analysing other CSF components such as neurofilament light chain and neurogranin.

Research evidence

Nobuo Itoh et al surveyed a total of 570 cerebrospinal fluid (CSF) samples from a variety of diseases, including Alzheimer's disease (n=5236), non-AD-demented and non-demented diseases (n=5239), and normal controls (n=595) to quantitate levels of tau protein phosphorylated at serine 199 (CSF/phospho-tau199) by a recently established sandwich ELISA. They found out that the CSF/phospho-tau199 levels in the AD group were significantly elevated compared to those in all the other non-AD groups. Receiver operating characteristics curves showed that the diagnostic sensitivity and specificity for the AD group versus all the other non-AD groups using the CSF/phospho-tau199 were 85.2% and 85.0%, respectively. Furthermore, there was a significant positive correlation between CSF/phospho-tau199 and CSF/total-tau levels in the AD group. Elevated CSF/phospho-tau199 in the AD group was noted irrespective of age, gender, dementia severity, and number of apolipoprotein E4 alleles. Thus, they suggested that CSF/phospho-tau199 may be a novel and logical biomarker in supporting ante mortem diagnosis of AD.

Model-derived time-course plots of MMSE score (24 months) according to CSF biomarker status for two multicentre longitudinal studies (Alzheimer's Disease Neuroimaging Initiative (ADNI), n = 619; BioFINDER, n = 431)





ADNI (upper panel) cut-offs;
pTau/Aβ(1–42) = 0.025, tTau/Aβ(1–42) = 0.27, Aβ(1–42) = 977 pg/mL

BioFINDER (lower panel) cut-offs;
pTau/Aβ(1–42) = 0.022, tTau/Aβ(1–42) = 0.26, Aβ(1–42) = 1,100 pg/mL.

pTau and tTau cut-offs of 27 pg/mL and 300 pg/mL respectively, were used in both cohorts. Analyses shown with adjustment for age, sex, years of education but without adjustment for APOEε4 status and number of patients in each biomarker group at baseline is presented.

The biomarker positive group showed greater change in Mini-Mental State Examination (MMSE) score compared to the biomarker negative group.

Email: colchempath@gmail.com Tel: +94 (0) 76 704 4871 Website: ccpsrilanka.com

Issues with CSF biomarkers

The difficulties of specimen (CSF) collection via lumbar puncture

The differences in preanalytical sample handling
Tubes for collection, sample handling and sample storage conditions, in particular, have been noted as critical factors.These factors have also been highlighted as a possible reason for problems linked to inter-centre variability.The type of sampling and storage tubes used is an important source of variability because of the tendency of Aβ peptides to adsorb on plastic surfaces.

It has been proposed that there is parallel adsorption of CSF Aβ42 and Aβ40 onto the sampling tube surface, regardless of the type of plastic.It has also been found that the use of the CSF Aβ42/40 ratio rather than CSF Aβ42 alone contributes toward pre-analytical standardization, removing the effects of pre-analytical interfering factors, such as tube type, freeze/thaw cycles and CSF volumes.

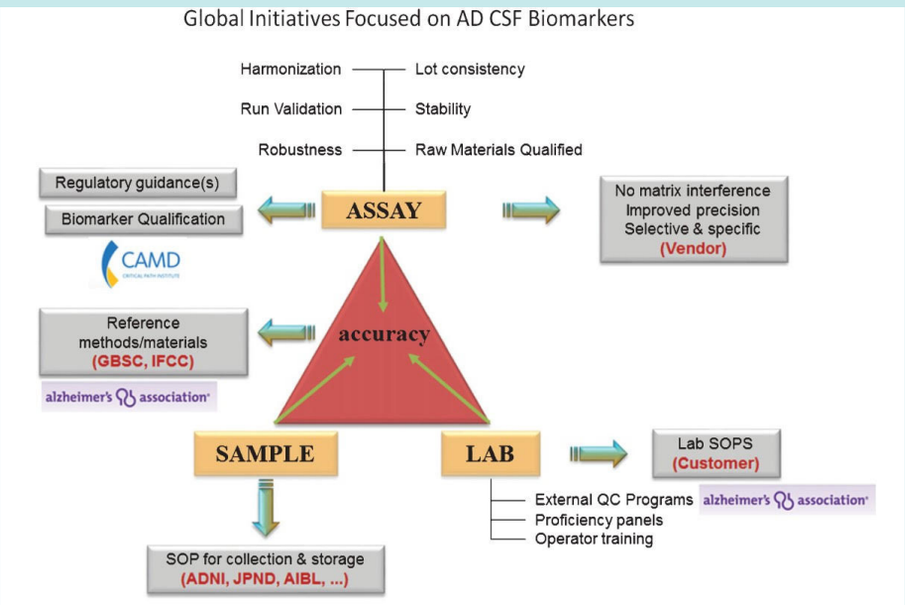
Lack of global standardization and harmonization of the available analytical methodologies and how to optimally analyze available data

Currently, immunoassays for CSF Aβ-42 suffer from between-laboratory and batch-to-batch variability and lack of standardisation across assays. As a consequence, no general cut-off values have been established for a specific context of use (clinical diagnostics) and selection of individuals for enrolment in clinical trials (patient stratification) remains challenging.

Two reference measurements procedures (RMPs) based on liquid chromatography tandem mass spectrometry for CSF Aβ-42 have been published and approved by the Joint Committee for Traceability in Laboratory Medicine (JCTLM).

Based on the commutability studies human CSF pools containing only endogenous Aβ1-42 at three concentrations were selected as the format for future CRMs.[14]

Global initiatives focused on CSF biomarkers for Alzheimer disease



Plasma biomarkers

The ability of measurement of amyloid-β precursor protein (APP)669–711/amyloid-β (Aβ)1–42 and Aβ1–40/Aβ1–42 ratios (high-performance plasma amyloid-β biomarkers) by immunoprecipitation coupled with mass spectrometry is demonstrated as minimally invasive, cost-effective blood-based biomarkers,potentially enabling broader clinical access and efficient population screening.

Even though these markers are supportive of the diagnosis of AD and less invasive, they are not recommended for routine diagnostic purposes yet because these assays are much less sensitive and specific.

The measurement of AD biomarkers (tau protein and Aβ 1–42), in blood samples may face analytical challenges due to their low abundance relative to the very high levels of plasma proteins, resulting in matrix interference, as well as possible biological confounders such as expression of these proteins in peripheral tissue with release into plasma.However, anticipating that once these biomarkers become more standardized they will be incorporated into clinical diagnostic algorithms for AD.

Genetic testing

The genetic testing is not recommended in the routine evaluation of patients with AD. APOE genotyping adds marginally to the predictive values of clinical criteria for AD.

Genetic testing for APP, PSEN1 and PSEN2 mutational analysis is commercially available but should be reserved for the cases in which young onset dementia occurs in the setting of a family history positive for an autosomal dominant distribution of early-onset cases.

Conclusions

The biochemical CSF markers can be used as aids for the diagnosis of AD and useful for the risk stratification and for the prediction of the disease progression. Though the use of plasma biomarkers is less invasive compared to CSF biomarkers, the serum assays are much less sensitive and specific and not recommended for clinical use yet.

Because of less number of request and per test cost it is not worthwhile to implement these biomarker panels in the routine laboratory setup. However, for complex clinical cases it is important to have a reference laboratory where theses samples can be sent to make the diagnosis more accurate.

References

1. Alzheimer A, Stelzmann RA, Schnitzlein HN, Murtagh FR. An English translation of Alzheimer's 1907 paper, "Uber eine eigenartige Erkankung der Hirnrinde". Clin Anat. 1995; 8:429–31.

2. Schultz C., Del Tredici K.H.B: Neuropathology of Alzheimer disease. InAlzheimer's Disease Current Clinical Neurology. Edited by R. R, B. R. Totowa,and NJ: Humana Press; 2004.

3. Aisen PS, Cummings J, Jack CR Jr, Morris JC, Sperling R, Frolich L, Jones RW, Dowsett SA, Matthews BR, Raskin J, et al. On the path to 2025: understanding the Alzheimer's disease continuum. Alzheimers Res Ther. 2017; 9:60.

4. Masters CL, Bateman R, Blennow K, Rowe CC, Sperling RA, Cummings JL. Alzheimer's disease. Nat Rev Dis Primers. 2015; 1:15056.

5. Lane CA, Hardy J, Schott JM. Alzheimer's disease. Eur J Neurol. 2018; 25: 59–70.

6. World AlzheimerReport2016.http://www.alz.co.uk/research/WorldAlzheimerReport2016.pdf. 2016.

7. Ballard C, Mobley W, Hardy J, Williams G, Corbett A. Dementia in Down's syndrome. Lancet Neurol. 2016; 15:622–36.

8. Ryman DC, Acosta-Baena N, Aisen PS, Bird T, Danek A, Fox NC, Goate A, Frommelt P, Ghetti B, Langbaum JB, et al. Symptom onset in autosomal dominant Alzheimer disease: a systematic review and meta-analysis. Neurology. 2014; 83:253–60.

9. Kang J, Lemaire HG, Unterbeck A, Salbaum JM, Masters CL, Grzeschik KH, Multhaup G, Beyreuther K, Muller-Hill B. The precursor of Alzheimer's disease amyloid A4 protein resembles a cell-surface receptor. Nature. 1987; 325:733–6.

10. Olsson B, Lautner R, Andreasson U, O¨ hrfelt A, Portelius E, Bjerke M, H¨oltt¨a M, Ros´en C, Olsson C, Strobel G, Wu E, Dakin K, Petzold M, Blennow K, Zetterberg H (2016) CSF and blood biomarkers for the diagnosis of Alzheimer's disease: A systematic review and meta-analysis. Lancet Neurol 15, 673-684.

11. Hardy JA, Higgins GA. Alzheimer's disease: the amyloid cascade hypothesis. Science. 1992; 256:184–5.

12. Blennow K, Wallin A, Agren H, Spenger C, Siegfried J, Vanmechelen E. Tau protein in cerebrospinal fluid: a biochemical marker for axonal degeneration in Alzheimer disease? Mol Chem Neuropathol. 1995; 26:231–45.

13. Grundke-Iqbal I, Iqbal K, Tung YC, Quinlan M, Wisniewski HM, Binder LI. Abnormal phosphorylation of the microtubule-associated protein tau (tau) in Alzheimer cytoskeletal pathology. Proc Natl Acad Sci U S A. 1986; 83:4913–7.

14. Julia Kuhlmann J, Andreasson U, Pannee , Bjerke M, Portelius E, Andreas Leinenbach A, et al. CSF Aβ 1-42 - an excellent but complicated Alzheimer's biomarker - a route to standardisation. Review;Clin Chem Acta;2017 Apr;467:27-33. doi: 10.1016/j.cca.2016.05.014. Epub 2016 May 20.

15. Lewczuka P, Matzenc P, Blennowd K, Parnettie L, Molinuevof L, Eusebie P, et al. Cerebrospinal Fluid Aβ42/40 Corresponds Better than Aβ42 to Amyloid PET in Alzheimer's Disease. Journal of Alzheimer's Disease 55 (2017) 813–822.

Research and Audit

Utility of Aldosterone, Renin Activity, and Aldosterone-to-Renin Ratio Testing: An Audit at the National Hospital of Sri Lanka

Samarakoon SMPP[1], Basnayake BMTK[1],
Jayasekara D[1], Panapitiya N[2], Herath T[2], Katulanda G W[1]
[1]Department of Chemical Pathology, National Hospital Sri Lanka
[2]Medical Research Institute,Colombo

Introduction

Aldosterone concentration and plasma renin activity (PRA) are essential screening tests for primary hyperaldosteronism, a condition that can lead to significant comorbidities if left untreated [1]. This diagnostic evaluation, which includes measuring the aldosterone-to-renin ratio (ARR), is crucial for identifying patients who may benefit from targeted therapeutic interventions [2]. However, in a government hospital setting, the costs associated with these tests can be substantial. The typical diagnostic criteria involve PRA<1 ng/mL/hr or plasma renin activity combined with a plasma aldosterone concentration (PAC) >15 ng/dL. If these criteria are met, especially in the presence of hypokalaemia [3] or resistant hypertension, further confirmatory testing like saline loading might be unnecessary [4]. This audit aims to assess the impact of ARR testing at the National Hospital of Sri Lanka, considering its availability, cost, and subsequent influence on patient management.

Background

The National Hospital of Sri Lanka handles over 800,000 clinic visits annually, with over 70,000 dedicated to endocrine disorders. Given the high volume of patients and the significant costs associated with ARR testing, it is crucial to evaluate the use of these tests comprehensively. This audit seeks to understand the frequency of ARR testing, the demographic distribution of patients undergoing these tests, and the follow-up actions based on test results.

Method

This retrospective, descriptive audit analysed ARR testing reports from January 1, 2024, to May 30, 2024, for patients referred from various units within the National Hospital of Sri Lanka. Data collected included patient demographics, test results, and follow-up actions. The audit aimed to determine the prevalence of ARR testing among hypertensive patients, the proportion of test results indicating primary hyperaldosteronism, and the rate of follow-up and subsequent management.

Results

During the audit period, 167 patients underwent ARR testing. All patients were hypertensive, and a significant majority, 86% (n=143), presented with hypokalaemia. The patient demographics were as follows: Out of them 47.9% (n=80) were females, and 52.09% (n=87) were males (figure 2). The age distribution was: 1.19% (n=2) below 20 years, 40.71% (n=68) between 20-40 years, 41.91% (n=70) between 40-60 years, and 16.16% (n=27) over 60 years (figure 1).

Email: colchempath@gmail.com Tel: +94 (0) 76 704 4871 Website: ccpsrilanka.com

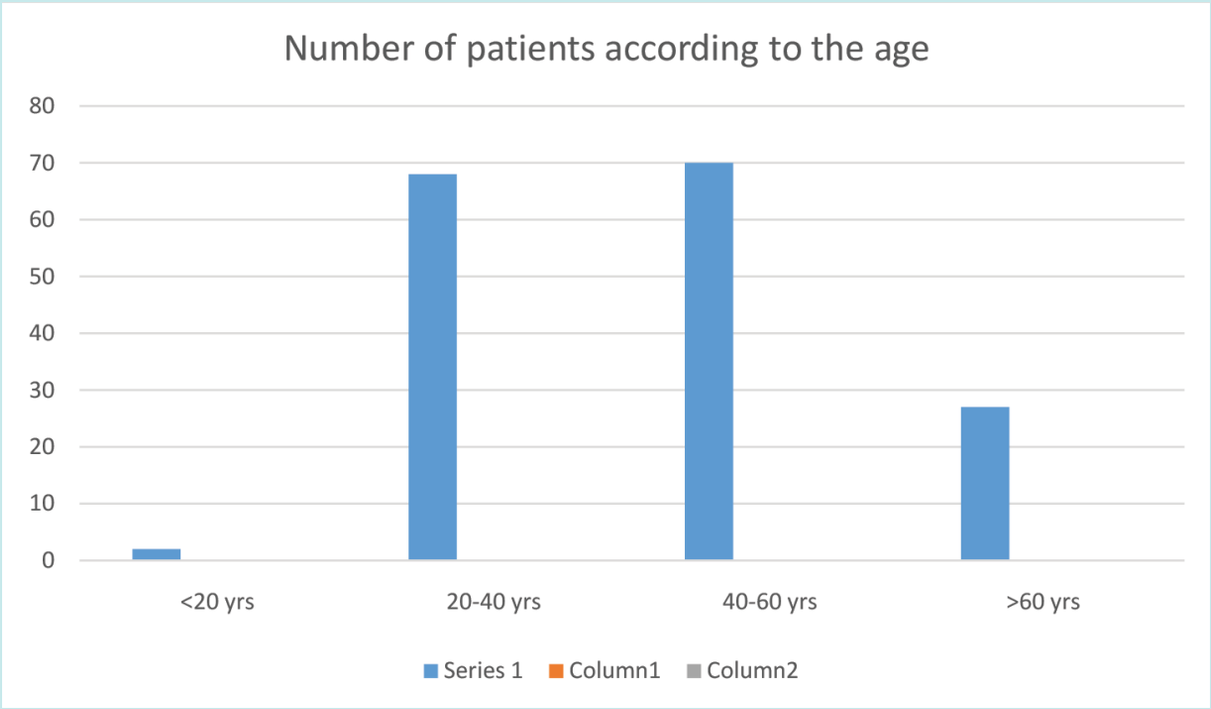


Figure 1.

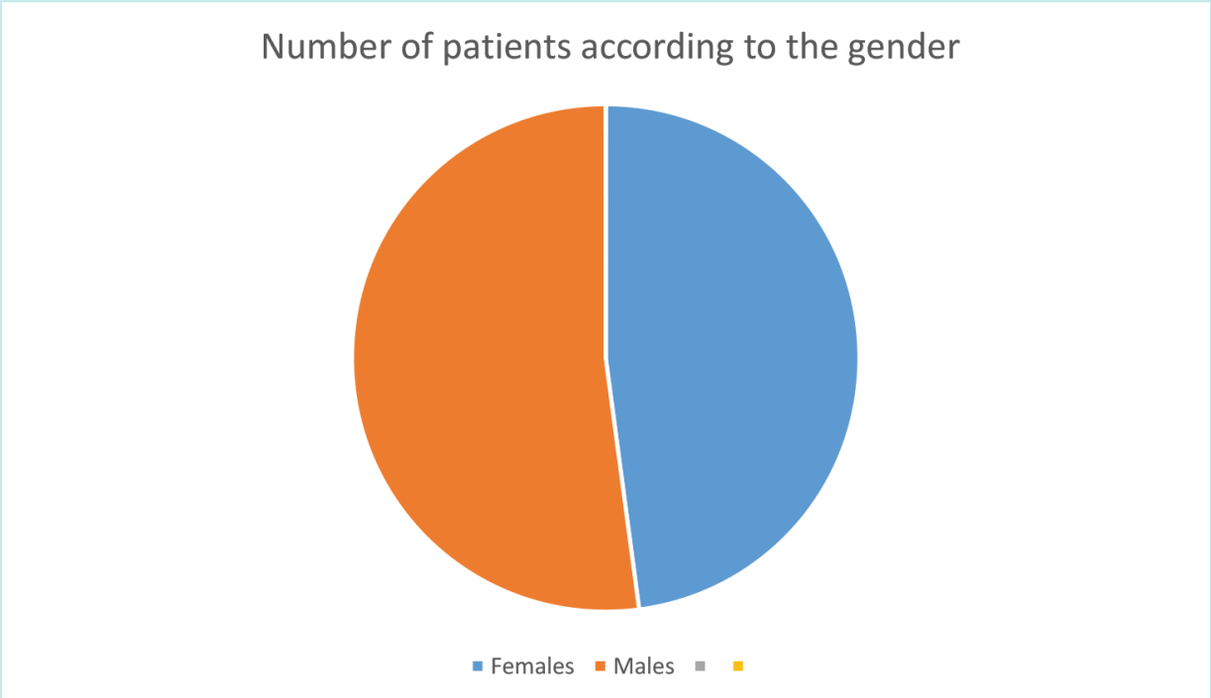


Figure 2.

Among the 167 patients, 54 had a renin level <1 ng/mL/hr. Of these, 35.1%(n=19) patients, had an aldosterone level >15 ng/ dL while 51.85 %(n= 28) number of patients had aldosterone concentration between 5 to ng/dL to 15 ng/ dL. Moreover 18.51% (n=10) of the patients had aldosterone < 5 ng/dL (figure 3).

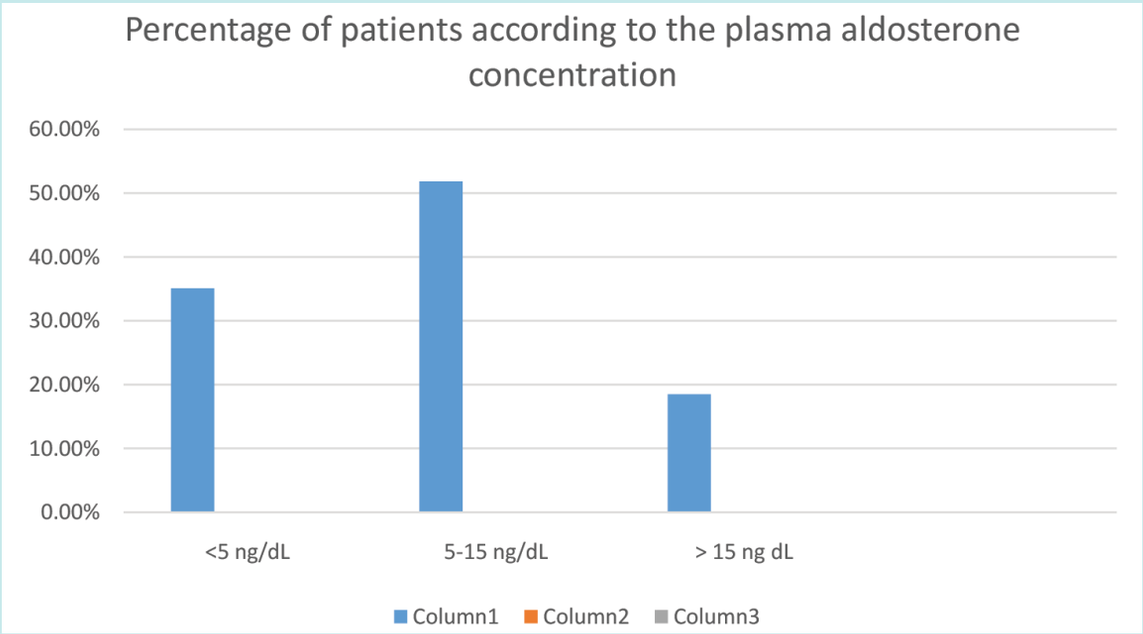


Figure 3.

Report collection was notably inconsistent. Only 36.05% (n=53) of the reports were retrieved by patients, while 63.95% (n=94) were not collected within 3 months (figure 4). Among the uncollected reports, 13.82% (n=13) showed renin <1 ng/mL/hr and aldosterone >10 ng/dL.

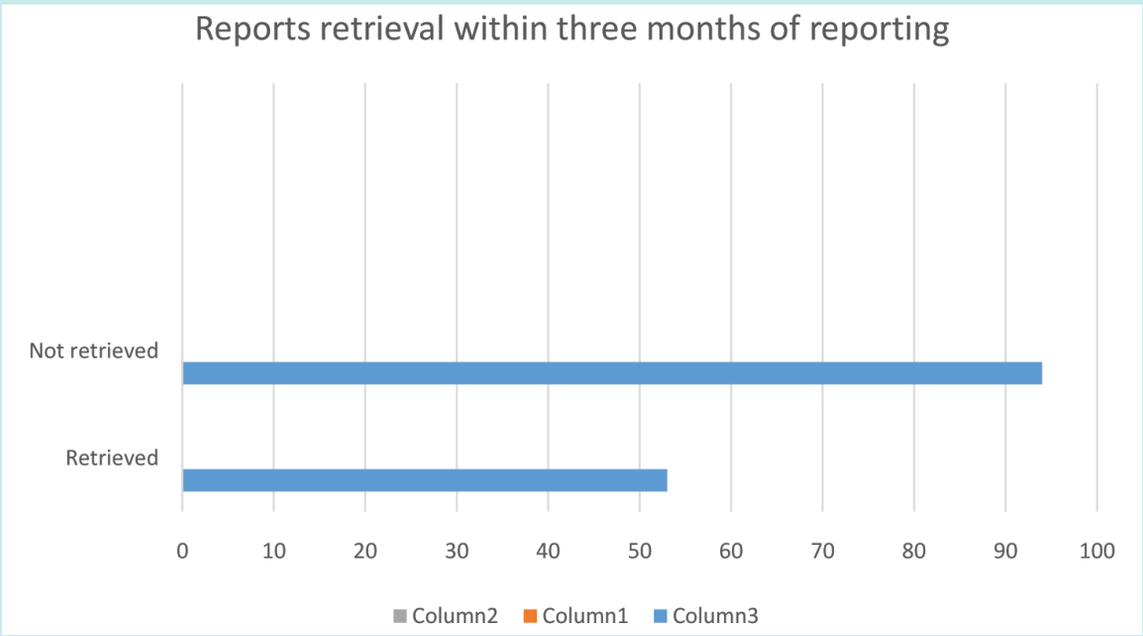


Figure 4.

For those who collected their reports, follow-up revealed that patients had undergone various management actions: the patients who had aldosterone concentration between 5-15 ng/dL were suggested to do confirmatory testing. Patients who got diagnosed with primary hyperaldosteronism were managed with medical treatment or planned

Email: colchempath@gmail.com Tel: +94 (0) 76 704 4871 Website: ccpsrilanka.com

to get adrenal venous sampling (AVS) done for subtyping. This ongoing study is in the process of documenting to get the exact statistics of the follow up patients.

Discussion

The audit highlights the critical role of PRA and PAC in the diagnostic process for hypertension and primary hyperaldosteronism. The results confirm that ARR testing is an effective screening tool, as evidenced by the proportion of patients with suppressed renin and elevated aldosterone levels.

Out of the 167 patients who underwent ARR at NHSL, nearly 80% showed diagnostic results or needed confirmatory testing. A minor percentage had PA excluded biochemically. This shows that good pre-test screening is in place.

However, the inconsistent report collection suggests a gap in patient follow-up, which could delay diagnosis and treatment. The laboratory is planning to implement a procedure to contact patients or referring clinicians to deliver reports.

The findings also emphasize the importance of cost-effective use of ARR testing. Given the financial constraints in a government healthcare setting, optimizing test utilization and follow-up protocols can enhance patient outcomes and reduce unnecessary expenditures.

Conclusion

The audit at the National Hospital of Sri Lanka demonstrates that PRA, PAC, and ARR testing are invaluable for diagnosing primary hyperaldosteronism in hypertensive patients. Proper use and follow-up of these tests are crucial for effective disease management and prevention of complications. Addressing the challenges related to report collection and improving follow-up procedures could further enhance the diagnostic and therapeutic processes, ensuring better patient care and resource utilization.

References

1. Reincke M, Bancos I, Mulatero P, Scholl UI, Stowasser M, Williams TA. Diagnosis and treatment of primary aldosteronism. The Lancet Diabetes & Endocrinology. 2021 Dec 1;9(12):876–92

2. Primary Aldosteronism Guideline Resources [Internet]. [cited 2024 Sep 10]. Available from: *https://www.endocrine.org/clinical-practice-guidelines/primary-aldosteronism*

3. Yoshida Y, Shibata H. Recent progress in the diagnosis and treatment of primary aldosteronism. Hypertens Res. 2023 Jul;46(7):1738–44.

4. Choy KW, Fuller PJ, Russell G, Li Q, Leenaerts M, Yang J. Primary aldosteronism. BMJ. 2022 Apr 20;377:e065250.

A preliminary study to determine a factor to make serum alkaline phosphatase values comparable between two ALP assays using different buffers; AMP and DEA

Jayasekara LMDT[1], Madanayake S[1], Thowfeek ZTM[1], Kulasinghe M[1], Fernando KKM[1, 2], Senevithilake K[1], Dayanath BKTP [1]

[1] Department of Chemical Pathology, Colombo North Teaching Hospital, Ragama

[2] Department of Biochemistry and Clinical Chemistry, Faculty of Medicine, University of Kelaniya

Introduction

Alkaline phosphatases (ALPs) are present in many tissues such as liver, bone, kidney, intestines, placenta. ALP hydrolyses organic phosphate esters and needs essential cofactors, zinc and magnesium. ALP is an analyte used in diagnosis of bone and liver pathologies.

Total ALP levels are analyzed using enzymatic, colorimetric assays in routine biochemistry laboratories using automated or semiautomated biochemistry analyzers based on spectrophotometry.

The enzymatic, colorimetric assay using 4-nitrophenyl phosphate (4-NPP) as the substrate and 2-amino-2-methyl-1-propanol (AMP) buffer at a pH of 10.4 is recommended as the reference method by the American Association for Clinical Chemistry (AACC), International Federation of Clinical Chemistry (IFCC)[1,2] and is enlisted in the Joint Committee for Traceability in Laboratory Medicine (JCTLM) database[3]. Another enzymatic, colorimetric assay using the same substrate (4-NPP) and a different buffer named diethanolamine (DEA) buffer at pH 9.8 is commercially available[4] and is recommended by the Scandinavian Society for Clinical Chemistry (SSCC) as the reference method[5].

It is observed that DEA-based assays give higher ALP values compared to AMP-based assays[6]. The objective of this study is to determine a factor between these two assays.

Materials and Methods

The study was conducted at the Department of Chemical Pathology, Colombo North Teaching Hospital (CNTH), Ragama in 2024. Samples were identified by the laboratory generated sample specific barcode.

Assay 1 is with dedicated reagents for the automated analyzer in the department,using AMP buffer (435 mmol/L), 4-NPP substrate (50 mmol/L), magnesium acetate, zinc sulphate, with a linearity range of 5-800 U/L. The assay is monitored with internal and external quality control program.

Assay 2 is from a different supplier using DEA buffer (3500 mmol/L), 4-NPP substrate (45 mmol/L), magnesium chloride with linearity range of 9.8-1600 U/L. The internal quality control was monitored during the study period.

The routinely analyzed samples for ALP with assay 1 were subjected to reflex analysis with assay 2 on the same automated biochemistry analyzer, having less than 30-minute gap between measurements over a period of 2 weeks to include possible variations in reagents, instruments and the operators.

Results

150 patient samples were included in the study. The correlation graph between the two assays had a high R^2 of 0.975 indicating an adequate number and spread of samples in the AMP based ALP range of 28-540 U/L. Bland Altman plot indicated increasing difference with increasing concentration with a mean difference of 135.7 U/L. But relative difference of difference (Rel DoD) plot revealed there is no such increasing difference with increasing concentration. The mean ratio of ALP values assay 2/ assay 1 was 2.1, having no significant change over the ALP range studied. Hence, the ALP values from DEA based assay needs to be divided by 2.1 to make them comparable to AMP based assay.

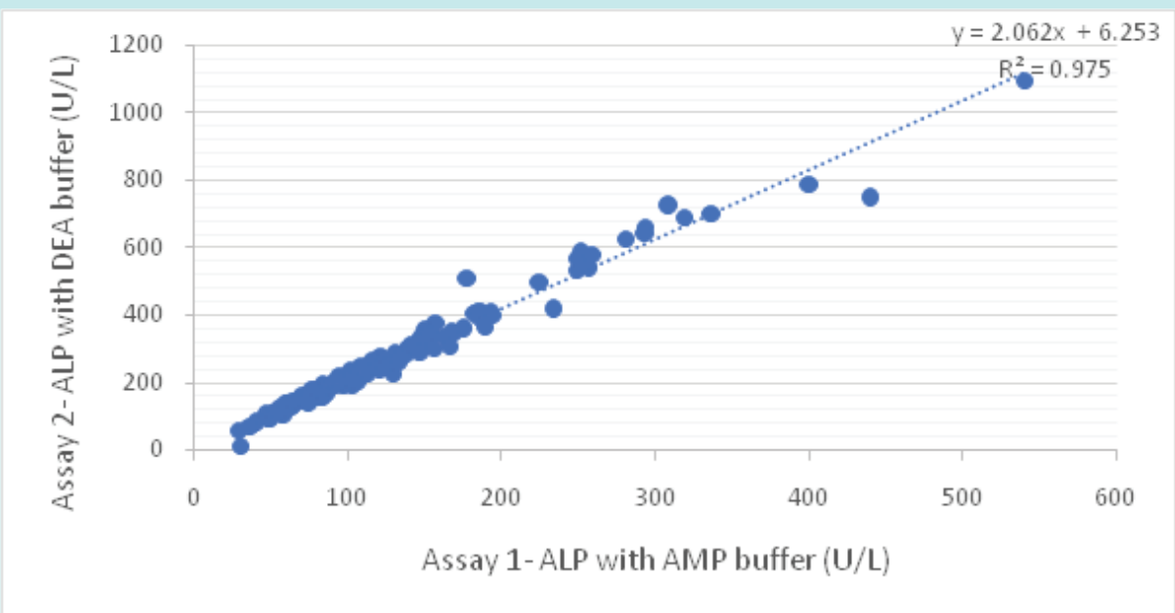


Figure 1-Correlation graph between ALP values by assay 1 (AMP based) and assay 2 (DEA based).

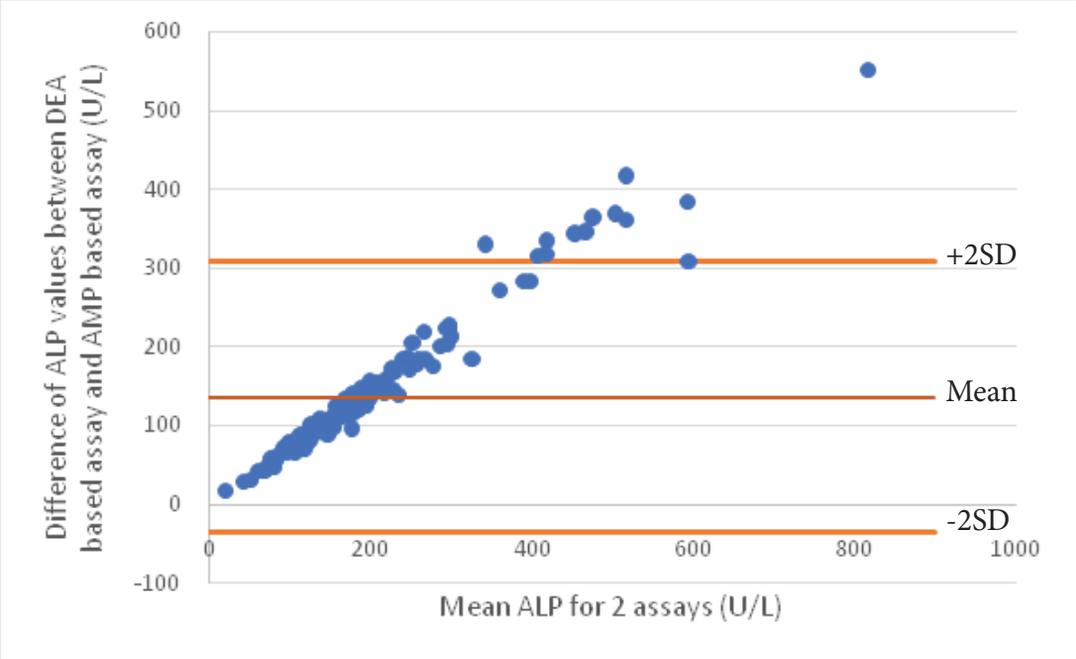


Figure 2- Bland Altman plot indicating rising difference of ALP between two assays with increasing concentration.

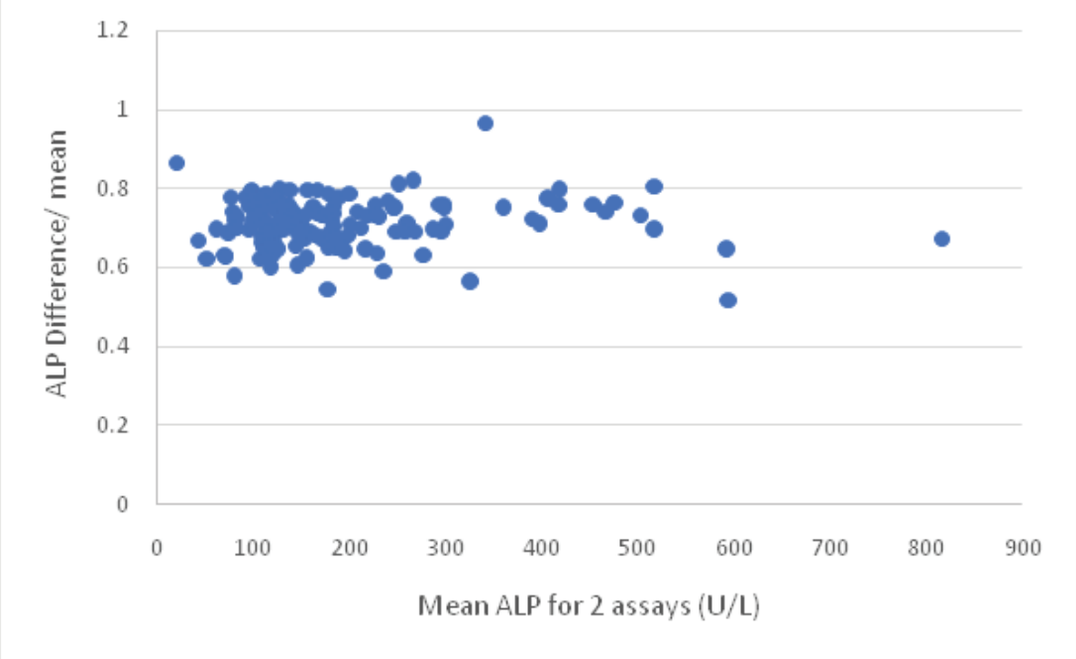


Figure 3- Relative Difference of Difference plot indicating lack of significant rise in difference of ALP values between two assays with rising concentration.

Email: colchempath@gmail.com Tel: +94 (0) 76 704 4871 Website: ccpsrilanka.com

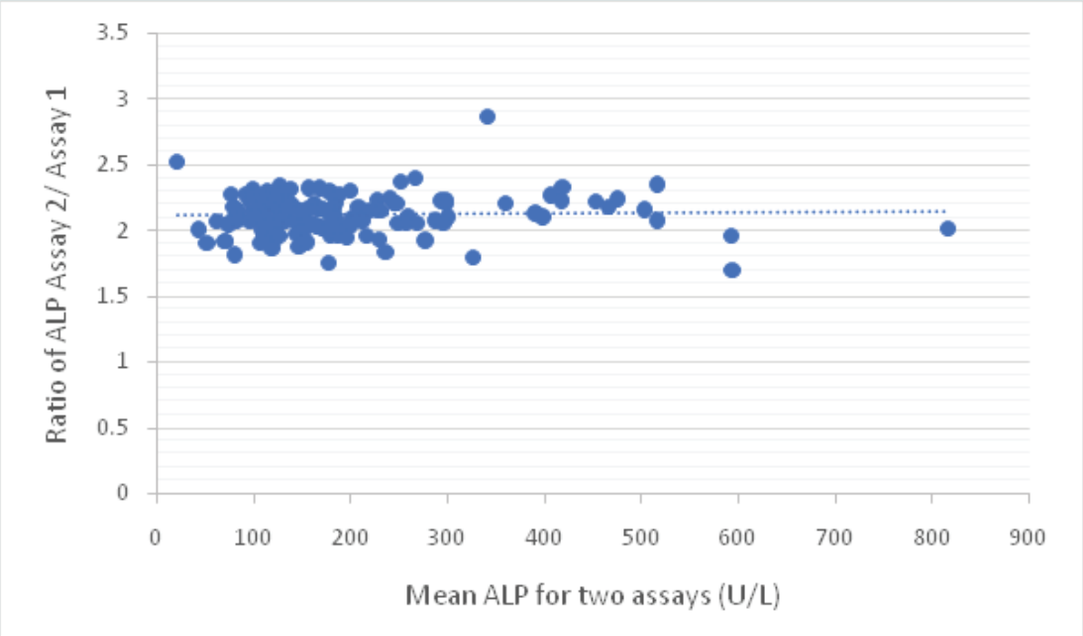


Figure 4- Ratio of ALP between DEA-based/ AMP-based assay is constant at 2.1 across concentration range.

Discussion

Using different buffers for ALP is extensively studied worldwide and found to have different ALP enzyme activities with different buffers at different buffer concentrations[7,8].

There are only limited studies published in relation to developing factors between ALP assays with AMP and DEA buffers.One such study using 106 samples have revealed a 2.47 ratio between DEA/ AMP ALP assays in Italy[9]. Another study in India using 250 samples has revealed a factor of 2.47 between ALP assays using DEA and AMP buffers using same analyzer and same company reagents which differ only from the buffer [6]. It is reported that even there is a significant difference between different AMP based-ALP assays as well, elucidating there are many factors influencing the ALP activity[10].

Another study has shown that incubation with AMP buffer causes loss of ALP activity, but not with DEA buffer [11], elaborating a possible etiology for the difference observed.

It is shown that if commutable calibrators are used, the AMP and DEA buffer based ALP assays can be made comparable[9], providing with analternative solution for ALP value harmonization, rather than factor correction.

Strengths of this study are using patient samples mimicking the practical set up, over a wider range of ALP values, using the same automated biochemistry analyzer avoiding possible other analytical variabilities and having a minimal gap between analysis by two assays eliminating the pre-analytical variation of rising ALP activity with storage[12].

The main limitation of this study is, the two assays being from different suppliers having differences in cofactors included as reagents, though the same substrate is used. Ideally the comparison should be between assays from the same supplier where buffer is the only difference.

Conclusion

This study showcases that when two ALP assays with different buffers need harmonization by applying a factor correction, it is advisable to develop the factor using an adequate number of samples. Our study indicates a factor of 2.1 for the ALP values by DEA-based/ AMP-based assays.

References

1. Tietz NW, Burtis CA, Duncan P, Ervin K, Petitclerc CJ, Rinker AD, et al. A reference method for measurement of alkaline phosphatase activity in human serum. Clin Chem. 1983 May;29(5):751–61.

2. Schumann G, Klauke R, Canalias F, Bossert-Reuther S, Franck PFH, Gella FJ, et al. IFCC primary reference procedures for the measurement of catalytic activity concentrations of enzymes at 37 °C. Part 9: Reference procedure for the measurement of catalytic concentration of alkaline phosphatase: International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Scientific Division, Committee on Reference Systems of Enzymes (C-RSE) 1). Clinical Chemistry and Laboratory Medicine. 2011 Sep 1;49(9):1439–46.

3. JCTLM Database [Internet]. [cited 2024 Sep 10]. Available from: https://www.jctlmdb.org/#/app/search/search-results?keywords=alkaline%20phosphatase&code_type=rmp

4. Viitala AJ, Jokela HA, Penttilä IM, Nummi S. A continuous-flow method for the determination of the activity of serum alkaline phosphatase in diethanolamine buffer. Scand J Clin Lab Invest. 1975 May;35(3):267–73.

5. Recommended methods for the determination of four enzymes in blood - PubMed [Internet]. [cited 2024 Sep 10]. Available from: https://pubmed.ncbi.nlm.nih.gov/4369123/

6. S R, M G, D AK, R D, S S. Comparison of alkaline phosphatase assay using two different buffer systems: AMP and DEA. World Journal of Pharmaceutical Sciences. 2015 Jul 6;1446–9.

7. McComb RB, Bowers GN Jr. Study of Optimum Buffer Conditions for Measuring Alkaline Phosphatase Activity in Human Serum. Clinical Chemistry. 1972 Feb 1;18(2):97–104.

8. Lewandrowski K, Lee-Lewandrowski E, Bowers GN, McComb RB. Investigation of N-Methyl-D-Glucamine Buffer for Assay of Alkaline Phosphatase in Serum. Clinical Chemistry. 1992;38(11):2286.

9. Cattozzo G, Albeni C, Franzini C. Harmonization of values for serum alkaline phosphatase catalytic activity concentration employing commutable calibration materials. Clinica Chimica Acta. 2010 Jun 3;411(11):882–5.

10. Lamb EJ, Browne M, John WG, Price CP. Alkaline phosphatase activity measurement in the UK by AMP-buffered methods: an appraisal of current practice. Ann Clin Biochem. 1998 Jan;35 (Pt 1):120–7.

11. Pekelharing JM, Leijnse B. Initial activity and inactivation of alkaline phosphatase in different lots of buffer. Clin Chim Acta. 1978 May 2;85(3):335–8.

12. Lowe D, Sanvictores T, Zubair M, John S. Alkaline Phosphatase. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Sep 10]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK459201/

A Child with Liver Cell Disease

Dr Thayani Arooran
Registrar in Chemical Pathology
Lady Ridgeway Hospital for Children

Case presentation

A 10-year-old baby girl, first born child of non-consanguineous parents with uncomplicated birth history, normal growth and development, presented with gradual onset of facial puffiness and abdominal distension over 3 months which was worsening over last few days. She was icteric and abdominal examination revealed mild hepatomegaly without free fluids. Cardiovascular, respiratory and neurological examination findings were unremarkable.

Basic Investigations

Haematology	Result	Unit	Reference Interval
White cell count	7.4	10^3 /µL	4-10
Neutrophils	28	%	50-70
Lymphocytes	55	%	20-40
Monocytes	1.72	%	3-12
Eosinophils	0.79	%	0.5-5
Red cell count	4.66	10^6µ/L	3.5-5.5
Haemoglobin (Hb)	10.4	g/dL	11-16
Haematocrit	38	%	37-54
Mean corpuscular volume	86.3	fL	80-100
Mean corpuscular Hb	32.9	pg	27-34
Platelets	172	10^3 /µL	150-450
Blood picture	No evidence of ongoing haemolysis noted		
Prothrombin time (PT)	23.2	s	
INR	**1.77**		0.9-1.15
APTT	**60.7**	s	26-38
Biochemistry (serum)			
Creatinine	33	µmol/L	30-60
Sodium	140	mmol/L	135-145
Potassium	4.0	mmol/L	3.5-5.1
Total calcium	2.1	mmol/L	2.2-2.7
Albumin	**23**	g/L	34-50
Corrected calcium	2.44	mmol/L	2.2-2.7
Magnesium	0.9	mmol/L	0.6-1.0
Phosphorus	1.72	mmol/L	1.45-2.16
Alkaline phosphatase	241	U/L	60-425
Total protein	71	g/L	64-83

Creatine kinase	66	U/L	30-150
AST	**164**	U/L	0-40
ALT	**69**	U/L	9-48
Total bilirubin	**56**	µmol/L	3-20
Direct bilirubin	**43**	µmol/L	0-3
Gamma-glutamyl trans-ferase	**154**	U/L	2-30
C-reactive protein	19	mg/L	0-5
Triglycerides	1.50	mmol/L	0.51-2.38
Total cholesterol	5.33	mmol/L	2.88-5.23
25 (OH) vitamin D	20.3	ng/mL	10-30 Insufficient

Questions

1.What are the possible causes for chronic liver cell disease in this patient?

2.What are the special investigations to be performed in this patient?

3.These are the special investigation results. What is the most probable diagnosis of this patient?

Serum Iron	92	µg/dL	60-180
UIBC	224	µg/dL	155-355
TIBC	306	µg/dL	274-385
Iron saturation	30	%	15-50
C3	18.3	mg/dL	87-200
C4	21	mg/dL	19-52
Serum Ceruloplasmin	**14**	mg/dL	18-45
24 hr urine copper excretion	**3519.25**	µg/24 hrs	<53.9
Antinuclear antibody (ANA) titre 1:80	Negative		
Viral hepatitis screening	Negative		

4. Mention other investigations that can be done to support the diagnosis and assess complications in this patient?

5.What is the diagnostic scoring system for the disease you mentioned in question 3 and the score for this patient?

6.What are the treatment options available for this patient?

Answers

1.Chronic viral hepatitis

Wilson disease
Autoimmune hepatitis
Haemochromatosis

2. Hepatitis viral studies

Serum ceruloplasmin and urinary copper excretion
Serum iron studies
Complement levels

3.Wilson disease

4. Ultrasound scan abdomen
Upper gastrointestinal endoscopy

Genetic studies

Ultrasound scan Abdomen	Evidence of chronic liver cell disease No focal liver lesions Splenomegaly and mild ascites Evidence of portal hypertension
Liver biopsy	Micronodular cirrhosis with chronic hepatitis
Upper gastrointestinal endoscopy (UGIE)	Grade II esophageal varices, 3 columns banded. Rest of the stomach normal.
Genetic study	A heterozygous pathogenic variant and a heterozygous variant of uncertain significance were identified in *ATP7B* gene. The genetic diagnosis of autosomal recessive Wilson disease is possible.

5. Leipzig score-7

Test	Parameter	Score	Score of this patient
KF ring	present absent	2 0	0
Neurological symptoms	severe mild absent	2 1 0	0
Serum ceruloplasmin (g/L)	normal >0.2 0.1-0.2 < 0.1	0 1 2	1
Coombs-negative haemolytic anaemia	Present absent	1 0	0
Liver copper (in the absence of cholestasis)	>250 µg (>4 µmol) g^{-1}dry weight 50–249 µg (0.8–4 µmol) g^{-1} Normal: <50 µg (<0.8 µmol) g^{-1} Rhodanine-positive granules	2 1 -1 0	Copper stain not done
Urinary copper (in the absence of acute hepatitis)	Normal 1–2 × upper limit of normal (ULN) >2 × ULN Normal but >5 × ULN after D-penicillamine	0 1 2 2	2
Mutation analysis of *ATP7B*	Biallelic deleterious variants One deleterious variant No mutation detected	4 1 0	4
Total score evaluation ≥4 Diagnosis established 3 Diagnosis possible; more tests needed ≤2 Diagnosis very unlikely			

Email: colchempath@gmail.com Tel: +94 (0) 76 704 4871 Website: ccpsrilanka.com

5.

- Copper chelation therapy is the main modality along with dietary restriction of copper rich foods.
- Trientine and zinc sulphate to enhance the urinary copper excretion.
- Ursodeoxycholic acid, vitamin A, D, K supplementations
- Portal hypertension-endoscopy to identify oesophageal varies if present carvedilol.
- Regular follow up monitoring with endoscopy with prophylactic banding if varices present.

References

01. Eduardo Martínez-Morillo, Josep Miquel Bauça, Biochemical diagnosis of Wilson disease: an update, Adv Lab Med 2022; 3(2): 103–113.

02. Sánchez-Monteagudo, A, Ripollés, E, Berenguer, M. Espinós. C, Wilson disease: facing the Challenge of diagnosing a rare disease. Biomedicines 2021, 9, 1100, https://doi.org/10.3390/biomedicines9091100.

03. Richard K Gilroy, Praveen K Roy, Wilson disease, emedicine.medscape.com/article/183456.

04. Som Dev, Robert L. Kruse, James P. Hamilton, Svetlana Lutsenko, Wilson disease: update on pathophysiology and treatment, Front. Cell Dev. Biol. 10:871877. doi: 10.3389/fcell.2022.871877.

05. Jing Liu, Jing Luan, Xiaoyan Zhou, Yazhou Cui, Jinxiang Han, Epidemiology, diagnosis, and treatment of Wilson disease, Intractable & rare diseases research. 2017; 6(4):249-255. DOI: 10.5582/irdr.2017.01057.

06. Kasztelan-Szczerbinska, B, Cichoz-Lach, H, Wilson Disease: An update on the diagnostic workup and management. J. Clin. Med. 2021, 10, 5097. https://doi.org/10.3390/jcm10215097

A Patient with an Anterior Neck Lump

Dr D.W.D.Dinithi Madurangi
Registrar in Chemical Pathology
National Cancer Institute, Maharagama

Case presentation

A 41-year-old mother of 3, presented with an anterior neck lump for 6 months duration which was increasing in size. She has had an aunt with a thyroid carcinoma but the type of carcinoma is unknown. Her examination revealed blood pressure of 150/90 mmHg with pulse rate of 80 beats per minute. Neck examination revealed firm mass in right thyroid lobe which moved with swallowing and she had lymphadenopathy. She was clinically euthyroid.

USS - Inhomogeneous echogenic mass in right thyroid lobe, 3.2×1.9×1.7 cm^3 in size
Fine needle aspiration cytology – unsatisfactory specimen

Thyroid profile

- TSH – 2.05 mIU /L (0.4 – 4.05)
- fT4 – 1.2 ng/dL (0.8 – 2.0)
- Calcitonin level 246 pg/mL (1.0 – 4.8)

Patient underwent total thyroidectomy with cervical dissection and histology revealed a thyroid malignancy.

Questions

1. What is the most likely diagnosis in this patient?
2. Write two tumor markers to follow up this patient.
3. What are the common causes of elevated calcitonin?
4. What are the hereditary conditions associated with this malignancy?
5. How would you plan further investigations of this patient?
6. What is the genetic test to be done in this patient?
7. What is the TSH target to be maintained following surgery?
8. How would you plan family screening?

Answers

1.Medullary thyroid carcinoma
2. Calcitonin, CEA
3.Hypercalcaemia
Hypergastrinaemia
Neuroendocrine tumours
Renal insufficiency
Pulmonary disease
Chronic autoimmune thyroiditis
Prolong treatment with omeprazole, beta blockers, glucocorticoids
Heterophile antibodies

4. Familial medullary thyroid cancer
Multiple Endocrine Neoplasia Type 2A
Multiple Endocrine Neoplasia Type 2B

5. Medullary thyroid carcinoma can be inherited as a part of Multiple Endocrine Neoplasia Type 2 (MEN 2)

MEN 2A	MEN 2B
Parathyroid hyperplasia	Mucosal neuromas
Medullary thyroid carcinoma	Marfanoid body habitus
Pheochromocytoma	Medullary thyroid carcinoma
	Pheochromocytoma

Therefore we need to exclude other components of MEN 2 syndrome.

- 24-hour urine analysis for VMA, metanephrines
- PTH level
- Liver function test to exclude metastasis

6. RET protooncogene mutation

7. Initially TSH < 0.1 mIU/L
If disease free for 5-10 years 0.5-1.0 mIU/L

8. All patients with MTC, both apparently sporadic and those with a positive familial history, should undergo RET genetic screening. Once an RET mutation has been confirmed in an index patient, first-degree relatives should be screened rapidly to identify the 50% who inherited the mutation and are therefore at risk for development of MTC.

References

1.Yasir M, Mulji NJ, Kasi A. Multiple Endocrine Neoplasias Type 2. [Updated 2023 Aug 14]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK519054

2.Kim M, Kim BH. Current Guidelines for Management of Medullary Thyroid Carcinoma. Endocrinol Metab (Seoul). 2021 Jun;36(3):514-524. doi: 10.3803/EnM.2021.1082. Epub 2021 Jun 22. PMID: 34154310; PMCID: PMC8258323.

Activities in Brief (2024/2025)

Journal Clubs

On the 31st of January 2024, a thought-provoking journal club session on “Ethics for Laboratory Medicine” was conducted by Dr. D.C.L.Senevirathna a Registrar in Chemical Pathology at Teaching Hospital Karapitiya. The session explored the vital role of ethical principles in laboratory practices, focusing on topics such as patient confidentiality, informed consent, equitable resource allocation, and the ethical handling of diagnostic errors. The interactive discussion provided valuable insights into navigating ethical dilemmas in the evolving field of laboratory medicine, reinforcing its importance in patient care and scientific integrity.

Another Journal Club took place on the 3rd of April 2024, featuring a presentation by Dr. Y. Hemika, a Registrar in Chemical Pathology at Teaching Hospital Batticaloa. The topic was “Functional Assessment of Vitamin D Status by a Novel Metabolic Approach: The Low Vitamin D Profile Concept.” The presentation introduced a new metabolic approach to assess vitamin D levels, focusing on the Low Vitamin D Profile Concept, which aims to offer a more functional understanding of vitamin D deficiency beyond traditional measurement methods. This approach could provide deeper insights into the biological consequences of low vitamin D levels and their impact on health outcomes.

Hybrid Event

On the 24th of April 2024, a hybrid event took place at the Neurotrauma Auditorium of the National Hospital of Sri Lanka (NHSL). The event featured Prof. John Burnett, Consultant Chemical Pathologist at the University of Western Australia, who delivered an insightful lecture titled “Monogenic Chylomicronaemia: Deficiency of LPL and Related Factors.” The lecture covered advancements in understanding lipid metabolism disorders and their clinical implications.

Webinars

On the 20th of August 2024, a webinar was hosted by the College of Chemical Pathologists of Sri Lanka, focusing on “Biochemical Investigation in Subfertility & IVF.” The session was conducted by Prof Sumedha Wijerathna, Professor in Reproductive Biology, Faculty of Medicine, University of Colombo. The webinar discussed the latest diagnostic approaches in biochemical investigations related to infertility and assisted reproductive technologies, with a focus on clinical applications in IVF treatments.

Another educational webinar was held on the 5th of September 2024, with a focus on “Medical Negligence.” This session was led by Prof Sarathchandra Kodikara, Consultant Judicial Medical Officer at the University of Peradeniya. Prof Kodikara provided an in-depth analysis of legal aspects of medical negligence, covering case studies and guidelines for preventing malpractice in clinical practice.

On 16th October 2024, a webinar on "Lab Tests in Gastroenterology Practice" was conducted by Dr. Chinthaka De Silva, Consultant Gastroenterologist. The session focused on the crucial role of laboratory investigations in diagnosing and managing various gastrointestinal disorders, providing valuable insights for medical professionals.

Inaugural Badminton Tournament

On Saturday, the 7th of September 2024, the College of Chemical Pathologists of Sri Lanka held its inaugural badminton tournament. The event featured exciting matches in both the women's doubles and mixed doubles categories. Dr. Maduri Vidanapathirana and Dr Thathsarani Vithana Pathirana emerged as champions of the women's doubles, while Dr. Nesali Panapitiya and her partner Dr Akila Wijesundara clinched victory in the mixed doubles. The tournament provided a lively platform for members to engage in friendly competition, foster professional camaraderie, and promote physical wellness within the community.

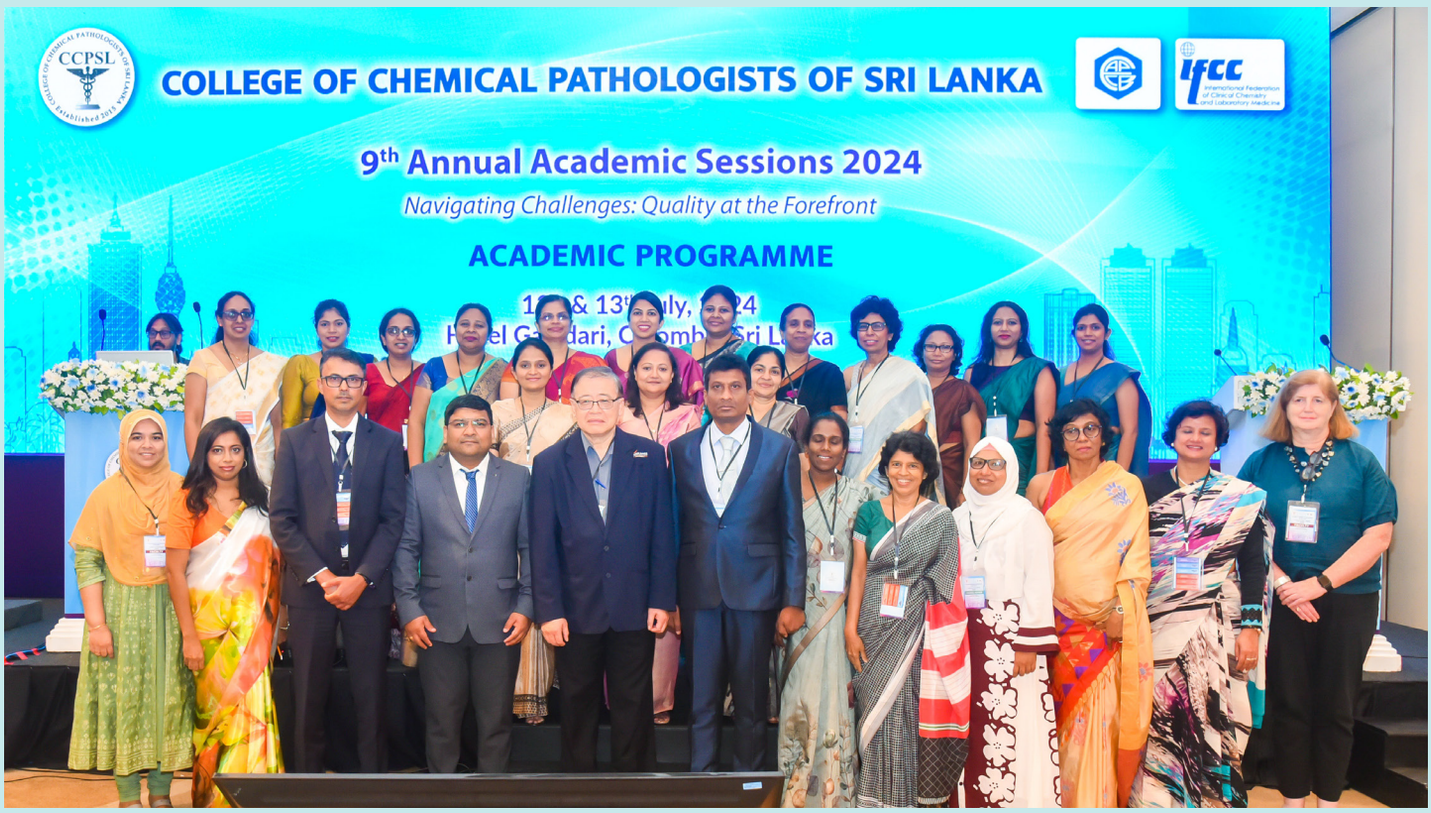
Email: colchempath@gmail.com Tel: +94 (0) 76 704 4871 Website: ccpsrilanka.com

Medical Laboratory Science Program

The College of Chemical Pathologists of Sri Lanka successfully hosted the Medical Laboratory Science Program on 25th and 26th November 2024 at the Samson Rajapakse Memorial Auditorium of the Sri Lanka College of Obstetricians and Gynaecologists, No. 112, Model Farm Road, Colombo 08. The program provided an enriching platform for advancing professional knowledge and skills in the field.

Sri Lankan Representation at APFCB Congress 2024

The 17th Asia-Pacific Federation for Clinical Biochemistry and Laboratory Medicine (APFCB) Congress took place at International Convention Centre Sydney, Australia from 31st October to 3rd November 2024. Sri Lanka was proudly represented by Dr. Thushara Hewageegana, Dr. Ganga Withana Pathirana, and Dr. Thathsarani Vithana Pathirana in the symposium titled "Chemical Pathology Investigations in Gastroenterological Disorders." Their participation contributed to the event's success and showcased Sri Lanka's expertise in Chemical Pathology.



Vitros® integrated systems are built to deliver accurate results, fast

Our integrated systems offer a full chemistry and immunoassay menu to meet a busy lab's testing needs on a single platform.

Efficiently consolidate critical testing to deliver quality, timely results to the clinicians and patients who depend on you

Simplify your lab by removing the need for plumbing, drains or water maintenance with Vitros waterless systems

Automate and streamline systems to allow your lab staff focus on the most critical tasks

CIC

Contact
Surin - 0715753434 /0765573434
Vivek- 0776992220

Email: colchempath@gmail.com Tel: +94 (0) 76 704 4871 Website: ccpsrilanka.com