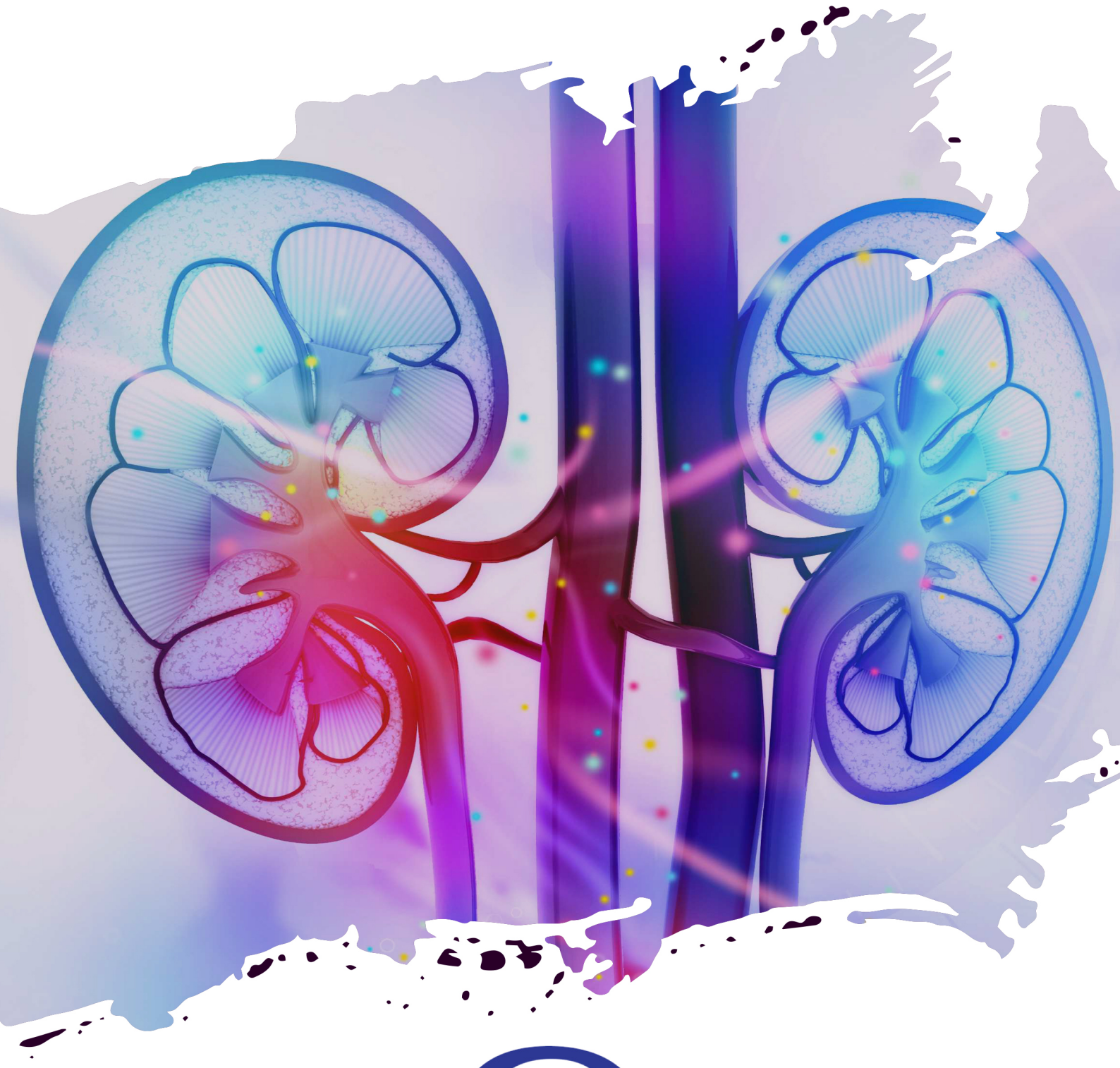
CHRONIC KIDNEY DISEASE

Recomendations for the Laboratory Reporting of eGFR and Urine Albumin

2019



MACB

Malaysian Association of Clinical Biochemists

Chronic Kidney Disease Task Force

(MACB CKD Task Force)

Foreword

The Malaysian Association of Clinical Biochemists (MACB) formed a Chronic Kidney Disease (CKD) Task Force that first met in December 2017. The aim of the MACB CKD Task Force was to survey the current practice of estimated glomerular filtration rate (eGFR) and urine albumin reporting in Malaysian laboratories and to produce recommendations on laboratory reporting of eGFR and urine albumin in order to promote uniformity and best practice amongst laboratories in Malaysia. The survey results and recommendations were presented at the 28th MACB Conference on 29th July 2018, to private pathology representatives and President of the Malaysian Society of Nephrology on 9th March 2019 as well as at the MACB-sponsored symposium at the 15th Asia-Pacific Congress of Clinical Biochemistry and Laboratory Medicine held in Jaipur, India on 19th November 2019. The recommendations were also circulated by email to nephrologists and family medicine specialists who were involved in producing the Ministry of Health of Malaysia Clinical Practice Guidelines on Management of Chronic Kidney Disease 2018 (second edition). All the comments received were taken into consideration in the MACB CKD Task Force recommendations on laboratory reporting of eGFR and urine albumin.

Dr Leslie Charles Lai Chin Loy
Chair, MACB CKD Task Force
20 November 2019

Recommendations for the Laboratory Reporting of eGFR and Urine Albumin

The following are the recommendations of the MACB CKD Task Force for the laboratory reporting of eGFR and urine albumin after presenting and discussing the recommendations at the 28th MACB Conference on 9th July 2018, Premiera Hotel, Kuala Lumpur and taking into consideration the comments made by participants at the conference as well as comments made during the joint meeting of the CKD Task Force members with the President of the Malaysian Society of Nephrology, Dr Sunita Bavanandan and representatives from the private pathology laboratories on 9 March 2019 at Pantai Hospital Kuala Lumpur. These recommendations were also circulated by email to nephrologists and family physicians involved in producing the Ministry of Health of Malaysia Clinical Practice Guidelines on Management of Chronic Kidney Disease 2018 (second edition) and their comments have been given due consideration in the recommendations of the MACB CKD Task Force.

These recommendations are based on the following guidelines:

a) Kidney Disease Improving Global Outcomes (KDIGO) 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease.[1]
b) National Institute for Health and Care Excellence (NICE) 2014 Clinical Guideline on "Chronic Kidney Disease in Adults: Assessment and Management".[2]

Recommendations for laboratory reporting of estimated glomerular filtration rate (eGFR)

1. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation shall be used in the calculation of eGFR and not the Modification of Diet in Renal Disease (MDRD) equation.

CKD-EPI creatinine equation
Female
if serum creatinine **≤ 62 µmol/L**
$eGFR\ (mL/min/1.73m^2) = 144 \times ((S.Cr \times 0.0113) / 0.7))^{-0.329} \times 0.993^{Age}$
if serum creatinine **>62 umol/L**
$eGFR\ (mL/min/1.73m^2) = 144 \times ((S.Cr \times 0.0113) / 0.7))^{-1.209} \times 0.993^{Age}$

Male
if serum creatinine ≤80 umol/L
$eGFR\ (mL/min/1.73m^2) = 141 \times ((S.Cr \times 0.0113) / 0.9))^{-0.411} \times 0.993^{Age}$
if serum creatinine >80 umol/L
$eGFR\ (mL/min/1.73m^2) = 141 \times ((S.Cr \times 0.0113) / 0.9))^{-1.209} \times 0.993^{Age}$

Multiply the value obtained by 1.159 if black

2. eGFR values ≤ 90 ml/min/1.73m^2 shall be reported as whole numbers.

3. eGFR values > 90 ml/min/1.73m^2 shall be reported as > 90 ml/min/1.73m^2.

4. eGFR shall be calculated for all creatinine measurements EXCEPT for people < 18 years of age and pregnant women.

5. Patients shall be advised to abstain from consuming any meat in the 12 hours before a blood test for serum creatinine as a protein meal can raise serum creatinine levels substantially and lead to low eGFR values.

6. Creatinine measurement shall be traceable to isotope dilution mass spectrometry (IDMS). A specific method for creatinine measurement (enzymatic method) is preferred. The analytical imprecision of the creatinine assay should be less than 3%, bias less than 4% and total allowable error less than 8.9%.[3]

7. Where a correction factor has been provided by a manufacturer to enable reporting of IDMS-traceable results for the Jaffe methods this correction factor shall be used to conform to the recommendation that all creatinine procedures have calibration traceable to the IDMS reference measurement procedure.

8. A correction factor shall be applied in the calculation of eGFR using the CKD-EPI equation for people of African-Caribbean or African family origin (multiply eGFR by 1.159 where creatinine is measured in SI units).

9. eGFR has to be interpreted with caution in people with extremes of muscle mass or certain illnesses (e.g. bodybuilders, people who have had amputations, muscle wasting disorders, acute myocardial infarction and acute kidney injury).

10. After the age of 30 years, glomerular filtration rate (GFR) progressively declines at an average rate of 8 ml/min/1.73m² per decade. There is considerable debate regarding the significance of this age-related decline in kidney function, which has been variously attributed to the effects of hypertension, atherosclerosis, or other comorbidities such as cardiovascular disease. Recent evidence suggests that even very elderly patients (>80 years of age) with modest reductions in eGFR (45–59 ml/min/1.73m²) have a higher prevalence of CKD-related complications compared to patients with an eGFR ≥60 ml/min/1.73m².

11. Serum creatinine must be measured within 12 hours of venepuncture as serum creatinine levels increase beyond 12 hours with the kinetic Jaffe method but not with the enzymatic method.

12. Laboratories using methods for creatinine measurement that are not IDMS-aligned shall not calculate eGFR using the IDMS-aligned CKD-EPI or MDRD equations as the values will be erroneous.

13. All laboratories that measure creatinine must participate in a national or an international external quality assessment scheme for creatinine.

The following are the KDIGO GFR categories:

GFR Category	eGFR (ml/min/1.73m^2)	Terms
G1	> 90	normal or high
G2	60 – 89	mildly decreased
G3a	45 – 59	mildly to moderately decreased
G3b	30 – 44	moderately to severely decreased
G4	15 – 29	severely decreased
G5	< 15	kidney failure

Recommendations for laboratory reporting of urine albumin

1. Albuminuria shall replace the term microalbuminuria.

2. Albumin to Creatinine Ratio (ACR) shall replace Protein to Creatinine Ratio (PCR) in the initial screening for proteinuria for the following reasons:
    I. ACR has greater sensitivity that PCR for low levels of proteinuria.
    II. Albumin measurement can be standardised and is more precise at low levels of proteinuria.
    III. Albumin is the predominant protein in the vast majority of proteinuric kidney diseases.
    IV. Total protein measurement is non-specific and subject to a range of false positive and false negative problems.

3. The first void urine in the morning shall be used for the measurement of ACR for the following reasons:
    I. Large day-to-day variation in urine albumin excretion of up to 40%.
    II. This variation is less with the first void urine sample in the morning than with a random urine sample.

4. For quantification and monitoring of large amounts of urine protein, > 70 mg/mmol, PCR may be used as an alternative.

5. PCR may be measured in hypertensive disorders of pregnancy, as stated in current NICE guidelines on hypertensive disorders of pregnancy, when there is significant proteinuria, i.e., when urine PCR is > 30 mg/mmol or a validated 24-hour urine collection result is > 300 mg protein.

6. ACR, and not PCR, is recommended for screening people with diabetes.

7. In the initial detection of proteinuria/albuminuria, if the initial urine ACR is between 3 and 70 mg/mmol this should be confirmed by measuring ACR on another early morning urine sample within 3 months. If the second urine sample is < 3 mg/mmol then a third early morning urine sample is required to confirm albuminuria (value > 3 mg/mmol) within 6 months of the first urine sample.

8. If the initial urine ACR is > 70 mg/mmol a repeat urine sample need not be tested.

9. A 24-hour urine albumin excretion rate may be measured to monitor patients after albuminuria has been confirmed but is not recommended for the initial detection of proteinuria/albuminuria.

10. A 24-hour urine albumin concentration alone shall not be reported but as part of a report of albumin excretion rate.

The following are the KDIGO categories of albuminuria:

ACR Categories	ACR (mg/mmol)	Terms
A1	< 3	normal to mildly increased
A2	3 – 30	moderately increased
A3	> 30	severely increased

At the meeting on 9 March 2019 Dr Sunita Bavanandan, President of the Malaysian Society of Nephrology drew attention to the fact that due to financial constraints the government hospitals will not be able to afford first-line screening of proteinuria using urine albumin to creatinine ratio. Hence, a modified algorithm is shown (Algorithm B) for use by institutions that have financial constraints. This is consistent with the recommendation of the 2018 Malaysian Clinical Practice Guidelines on Management of Chronic Kidney Disease.[4]

CKD Task Force members

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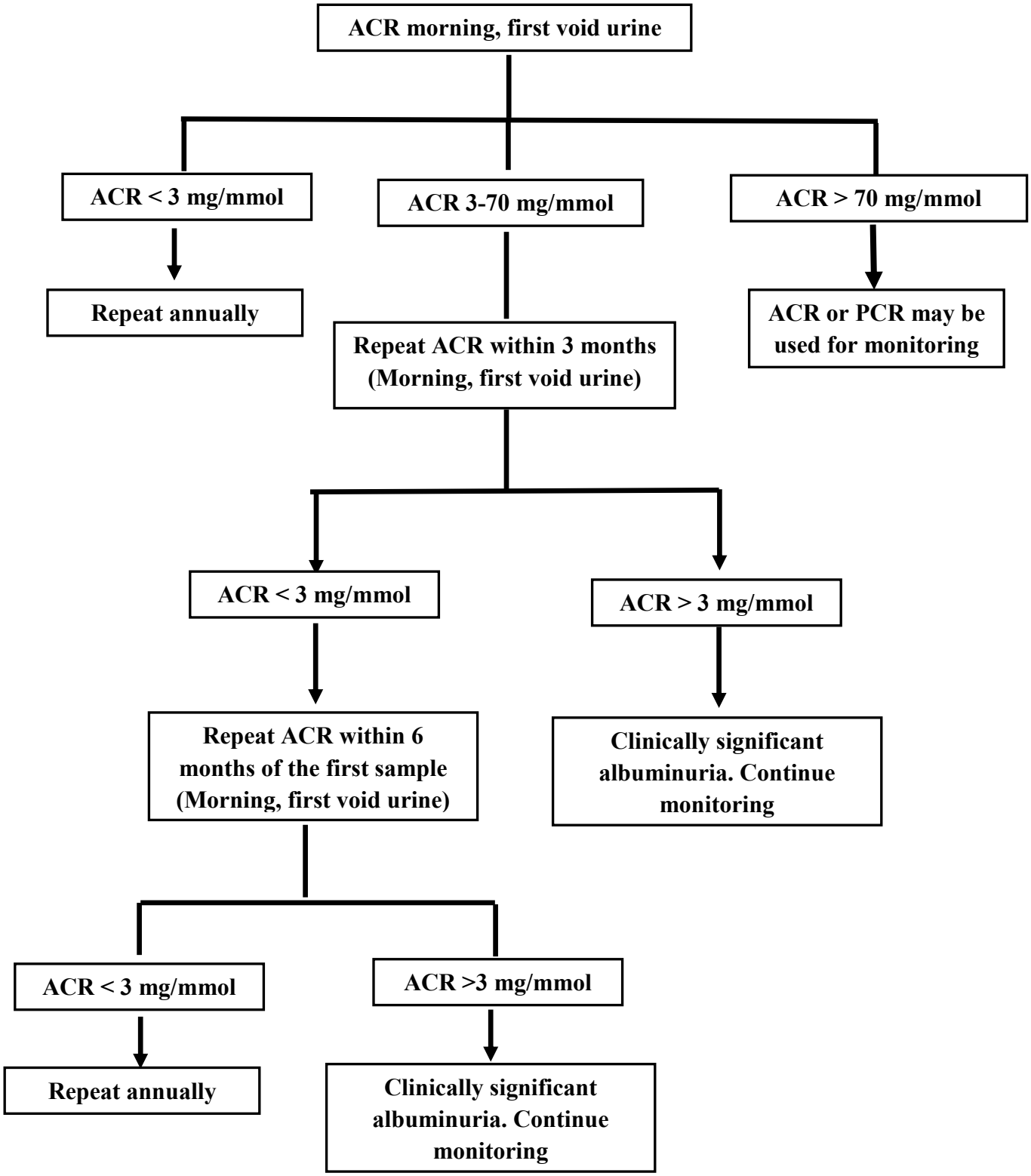
References

1. KDIGO 2012 Clinical Practice Guideline for the evaluation and management of chronic kidney disease. Kidney International (supplements) 2013; 3: 136-150.
2. Clinical Guidelines on Chronic kidney disease in adults: assessment and management. Published on 23 July 2014. nice.org.uk/guidance/cg182.
3. Desirable biological variation database specifications. Available at: https://www.westgard.com/biodatabase1.htm.
4. Clinical Practice Guidelines on Management of Chronic Kidney Disease (Second Edition, 2018). MOH/P/PAK/394.18 (GU).

ALGORITHM A

ASSESSMENT OF ALBUMINURIA IN CHRONIC KIDNEY DISEASE (CKD)



ALGORITHM B

REAGENT STRIP USED FOR INITIAL SCREENING FOR PROTEINURIA