Measured GFR (mGFR) and Estimated GFR (eGFR)

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RENAL FUNCTION ASSESSMENT

- ASSESSMENT OF GLOMERULAR FUNCTION
- ASSESSMENT OF TUBULAR FUNCTION
ASSESSMENT OF GLOMERULAR FUNCTION

- NONPROTEIN NITROGEN DETERMINATION
  - Serum Urea
  - Serum Creatinine

- DETERMINATION OF GLOMERULAR FILTRATION RATE
  - Creatinine Clearance
  - Estimated GFR (eGFR)
  - Cystatin C

- ASSESSMENT GLOMERULAR PERMABILITY
  - Proteinuria
  - Hematuria
NONPROTEIN NITROGEN (NPN)

- UREA (BUN)
- CREATININE
- URIC ACID
- AMMONIA
- AMINO ACIDS
SERUM UREA

- Produce During Catabolism of Amino Acids In Liver
- Excreted by Kidneys into Urine
UREMIA

- **PRERENAL**
  - High Protein Intake, Dehydration,
  - Decreased Renal Perfusion
  - (Shock, Hemorrhage, Congestive Heart Failure)
  - Drugs (Corticosteroids, Tetracycline)

- **RENAL**
  - Glomerular Disease, Tubular Disease,
  - Renal Failure

- **POSTRENNAL**
  - Nephrolithiasis, Genitourinary Tumors,
  - Prostate Enlargement
BLOOD UREA NITROGEN (BUN)

\[
O = C \quad \text{NH}_2
\]

\[
\text{UREA} = 60 \quad \text{BUN} = 28
\]

\[
\frac{\text{UREA}}{\text{BUN}} = \frac{60}{28} = 2.14
\]

\[
\text{UREA} = \text{BUN} \times 2.14
\]

\[
\text{BUN} = \frac{\text{UREA}}{2.14}
\]
UREA DETERMINATION

CHEMICAL (NONENZYMATIC) METHODS

- **Diacethyl Monoxime**
  - \( \text{Urea} + \text{Diacetyl} \rightarrow \text{Yellow Diazine} \)
  - \( \text{Addition of Thiosemicarbazide} \rightarrow \text{Pink Color} \)
  - \( \text{Thiosemicarbazide} & \text{Fe}^{2+} \rightarrow \text{Stability & Increased Intensity} \)

- **O-Phethaldehyde**
Specimens
- Serum, Urine

Urine
- Diacetyhl Monoxime Method

Increasing by Dietary Proteins & Activity

Inhibition of Urease by Flouride

Interference by Lipidemia, Hemolysis & Icterus

Urea Has Relative Stability
ENZYMATIC (INDIRECT) METHODS

Urea + H₂O → H₂CO₃ + NH₄⁺

- Nesslerization
  NH₄⁺ + Potassium iodide + Mercury iodide → Yellow-Pink Complex

- Berthelot
  NH₄⁺ + NaOCL + Phenol → Indophenol

- Indicator Dye

- Potentiometry

- Glutamate Dehydrogenase
  NH₄⁺ + α-KG + NADH + H⁺ → Glutamate + NAD⁺ + H₂O
## CV% OF EQAP: Urea

<table>
<thead>
<tr>
<th>Kit</th>
<th>87-1</th>
<th>87-2</th>
<th>88-1</th>
<th>88-2</th>
<th>88-3</th>
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<tbody>
<tr>
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<td>7.94</td>
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<td>17.33</td>
<td>14.35</td>
<td>17.82</td>
<td>18.34</td>
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<tr>
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<tr>
<td>Zi-M</td>
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<td>12.56</td>
<td>9.74</td>
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<td>-</td>
<td>9.62</td>
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<td>6.27</td>
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<td>6.45</td>
<td>8.57</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>3.8</td>
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<table>
<thead>
<tr>
<th>Average EQAP CV%</th>
<th>Allowable CV%</th>
<th>CCV%</th>
<th>Indian CCV%</th>
</tr>
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<tbody>
<tr>
<td>7.9</td>
<td>2.3</td>
<td>5.7</td>
<td>10.0</td>
</tr>
</tbody>
</table>

| 6.08 | 7.48 | 7.80 | 7.82 | 7.94 | 7.95 | 8.34 | 8.60 | 8.62 | 8.62 |
SERUM CREATININE

- It is produced in muscles and is excreted by kidneys.
- Nonrenal factors such as dehydration & protein catabolism have no significant effect on serum creatinine values.
- But it is affected by muscle mass, sex, race, diet, and tubular excretion.
CREATININE DETERMINATION

CHEMICAL (NONENZYMATIC) METHODS

- Alkaine Picric Reaction (Jaffe Method)
  1) *Interference with Proteins, Glucose, Ascorbate, Pyruvate, Acetoacetate, Acetone, Cephalosporins*
  2) *Using Ion Exchange Resins, Oxidation, Extraction, Acid Blank, Kinetic*
ENZYMATIC METHODS

Creatinase & Creatine Kinase

Creatinine + H₂O \[\xrightarrow{\text{Creatinase}}\] Creatine

Creatine + ATP \[\xrightarrow{\text{CK}}\] Creatine Phosphate + ADP

PEP + ADP \[\xrightarrow{\text{Pyruvate Kinase}}\] Pyruvate + ATP

Pyruvate + NADH + H⁺ \[\xrightarrow{\text{LDH}}\] Lactate + NAD⁺
Fasting is not Necessary
- Increased by Activity
- Stable
- Decreased in Urine with pH less than 4.9
- Hemolytic & Icterus Serums Are not Recommended
## CV% OF EQAP: Creatinine

<table>
<thead>
<tr>
<th>Kit</th>
<th>87-1</th>
<th>87-2</th>
<th>88-1</th>
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<th>90-1</th>
<th>90-2</th>
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<tbody>
<tr>
<td>Pa-A</td>
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<td>18.22</td>
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<td>18.51</td>
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<tr>
<td>Zi-M</td>
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<td>-</td>
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<td>15.24</td>
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<td>16.47</td>
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<td>9.73</td>
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<td>10.33</td>
<td>10.09</td>
<td>10.10</td>
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<tr>
<td>Ro-A</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>9.76</td>
<td>3.16</td>
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</table>

### Average EQAP CV% vs Allowable CV% vs CCV% vs Indian CCV% table:

<table>
<thead>
<tr>
<th>Average EQAP CV%</th>
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<th>Indian CCV%</th>
</tr>
</thead>
<tbody>
<tr>
<td>14.49</td>
<td>7.5</td>
<td>8.9</td>
<td>10.0</td>
</tr>
</tbody>
</table>

| 9.45 | 9.53 | 10.82 | 11.54 | 11.82 | 13.23 | 17.92 | 18.22 | 18.51 | 23.80 |
For Evaluation of Renal Diseases, Serum Urea & Creatinine Have

- Low Sensitivity
- Low Specificity
Serum Urea Nitrogen

Serum Creatinine

Normal Value  ➔  10 - 20

- Prerenal ➔  Increased
- Renal ➔  Normal
- Postrenal ➔  Increased
GLOMERULAR FILTRATION RATE (GFR)

- Is for Evaluation of Functional Nephron Mass
- Is for Monitoring of Renal Disease
- Is for Drug Dose Adjustment
- Is Calculated from Clearance

\[
\frac{U_S \text{ (mg/dL)} \times V_U \text{ (mL/min)} \times 1.73}{P_S \text{ (mg/dL)} \times A}
\]
Criteria for Ideal Substance in Clearance Determination

- **Constant Serum Concentration**
- **Ready Pass through Glomerular Filtration Barrier**
- **Neither Secreted Nor Reabsorbed**
- **Easy Measurement**
INULIN CLEARANCE

- Inulin Is A Fructosan
- Inulin Pass Readily through Glomerular Barrier And Has No Secretion & Absorption
- Is Reference Method
- Needs Continuous Injection
CREATININE CLEARANCE

- Creatinine production is relatively constant (with 15% daily variation)
- Creatinine has tubular secretion
  - Increase when GFR is low
  - Inhibited by salicylate, cimetidine, trimethoprim
- Needs 24h urine collection
UREA CLEARANCE

- Urea production is not relative constant
- Urea has tubular absorption → Underestimation
  - Decrease in GFR
    - Shock, Hemorrhage, Congestive Heart Failure
  - Drugs
    - Corticosteroids, Tetracycline
- Needs 24h Urine Collection
Estimated GFR (eGFR)

- 24h Urine Collection is not needed
- Is Based on Serum Creatinine Measurement and Correction for Weight, Age, Sex, and probably Race, Body Surface Area (BSA), or Renal Disease
Cockcroft – Gault (GC) Equation

- Was Published in 1976 by Cockcroft and Gault
- Is Based on Serum Creatinine Measurement and Correction for Weight, Age, and Sex

\[
eGFR = \frac{(140 - \text{age}) \times \text{Weight}}{72 \times \text{Serum Creatinine}}
\]

- Is Corrected for Female by multiplying 0.85
Modification of Diet in Renal Disease (MDRD) Equation

- Was Developed in 1999 by using patients who had CKD identified by elevated serum creatinine levels
- Is Based on Serum Creatinine Measurement and Correction for Weight, Age, and Sex

\[
eGFR = 186 \times \text{Serum Creatinine}^{-1.154} \times \text{age}^{-0.203} \times F
\]

- F is 0.742 for Female
In 2005, the Australasian Creatinine Consensus Working Group recommended that an eGFR based on the abbreviated MDRD formula be automatically calculated for every request for plasma creatinine in people over 18 years.
Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)

- Was Developed in 2009 by CKD-Epidemiology Collaboration group and intended to be more generalizable across various clinical settings than MDRD equation.
- Weight, diabetes, and transplant were considered as potential variables, but the final equation uses the same variables as the MDRD equation.
Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)

- Developed to match the accuracy of the MDRD equation at GFR < 60 mL/min/1.73m² and to offer greater accuracy at higher GFR, minimizing the over-diagnosis of CKD with the MDRD equation.
CKD-EPI

Serum Creatinine

eGFR = a x ( \frac{\text{Creatinine}}{b} ) c x (0.933)^\text{age}
Study In Spain Was Made on 84 Nondialyzed Patients with CKD in the Stage 4 or 5

<table>
<thead>
<tr>
<th>Method</th>
<th>Results (mL/min/1.73m²)</th>
<th>Correlation coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine Clearance</td>
<td>13.5 ± 5.1</td>
<td>-</td>
</tr>
<tr>
<td>Classic CG</td>
<td>14.2 ± 5</td>
<td>0.86</td>
</tr>
<tr>
<td>Corrected CG</td>
<td>12 ± 4.2</td>
<td>0.81</td>
</tr>
<tr>
<td>MDRD</td>
<td>12.1 ± 4.8</td>
<td>0.77</td>
</tr>
</tbody>
</table>

- In corrected CG, 0.84 is used as correction factor to compensate for the effect of tubular secretion of creatinine and make it closer to glomerular filtration.
- Classic CG equation is better than MDRD equation for estimating GFR in patients with advanced CKD.
Study In China Was Made on 7832 General Population

<table>
<thead>
<tr>
<th>Method</th>
<th>Results (mL/min/1.73m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDRD Equation</td>
<td>78.6 ± 21.3</td>
</tr>
<tr>
<td>CG Equation</td>
<td>71.5 ± 21.6</td>
</tr>
</tbody>
</table>

- MDRD mean was higher than CG mean
- This difference is higher in older
A study was made on 369 outpatients and inpatients over 20 years in Pakistan. The correlation coefficient with creatinine clearance when serum creatinine was less than 1.5 mg/dL was 0.608 for the CG Equation and 0.596 for the MDRD Equation. When serum creatinine was greater than 1.5 mg/dL, the correlation coefficient was 0.625 for the CG Equation and 0.724 for the MDRD Equation.
Study in Iran was made on 559 outpatients.

- Correlation coefficient with creatinine clearance

<table>
<thead>
<tr>
<th>Equation</th>
<th>All Ages</th>
<th>18-20 years</th>
<th>40-60 years</th>
<th>&gt; 60 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>CG</td>
<td>0.664</td>
<td>0.552</td>
<td>0.564</td>
<td>0.550</td>
</tr>
<tr>
<td>MDRD</td>
<td>0.727</td>
<td>0.644</td>
<td>0.614</td>
<td>0.691</td>
</tr>
<tr>
<td>CKD-EPI</td>
<td>0.722</td>
<td>0.598</td>
<td>0.619</td>
<td>0.697</td>
</tr>
</tbody>
</table>
Limitations of eGFR

- Is Not Suitable for GFR > 60 mL/min and < 15 mL/min
- Is Not Suitable for Children and Older
- Is Not Suitable for Vegetarians and Who Have Changed Body Mass
- Is affected by factors affecting on serum creatinine, creatinine excretion, and creatinine measurement
CYSTATIN C

- Is a low molecular protein with a molecular weight of 12.8 kDa and pI 9.2.
- Synthesized by all nucleated cells.
- Readily filtrated.
- Serum concentration depends on glomerular filtration and is not affected by diet, muscle mass, sex, age, and nonrenal conditions and diseases.
- Has more sensitivity for early stage of renal disease and in children and older.
- Not affected by interfering substances.