The sick parturient
Renal issues

Marlies Ostermann
Guy’s & St Thomas’ Hospital London
Normal - sub-clinical AKI - AKI I - AKI II - AKI III - Kidney failure

- Risk of non-recovery
- Risk of short and long-term complications
- Healthcare costs
Kidneys

Nephron

800,000 – 1Mio per kidney
Renal Physiology

Afferent artery

Efferent artery
Relatively small changes in pressure can affect ultrafiltration.
20% of CO + High GFR

→ High exposure to:
  toxins
  cytokines
  inflammatory products
Renal Physiology

KDIGO AKI guideline

Aims:
1. Consensus definition of AKI
2. Summary of best evidence management
### KDIGO definition of AKI

<table>
<thead>
<tr>
<th>Definition of AKI</th>
<th>Serum creatinine</th>
<th>Urine output</th>
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<tr>
<td></td>
<td>AKI is diagnosed if serum creatinine increased by ≥26.5µmol/l in ≤48h OR</td>
<td>&lt;0.5 ml/kg/h for 6 hours</td>
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<tr>
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<td>increased to ≥1.5-fold from baseline in the preceding 7 days</td>
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### KDIGO classification of AKI

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<th>Serum creatinine</th>
<th>Urine output</th>
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<tr>
<td>1</td>
<td>rise ≥ 26.5µmol/l in 48h OR 1.5-1.9 times from baseline</td>
<td>&lt;0.5ml/kg/h for 6-12h</td>
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<td>2</td>
<td>rise 2.0-2.9 times from baseline</td>
<td>&lt;0.5ml/kg/h for ≥12h</td>
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<tr>
<td>3</td>
<td>rise ≥ 3 times from baseline OR rise to ≥353.6µmol/l OR RRT irrespective of serum creatinine</td>
<td>&lt;0.3ml/kg/h for ≥24h OR anuria for ≥12h</td>
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Renal adaptation during pregnancy

**ANATOMICAL**
- Increase in kidney size (1 cm)
- Dilatation of the collecting system (R>L)

**GLOMERULAR HEMODYNAMICS**
- Vasodilation
- Increase in RPF and GFR

**TUBULAR FUNCTION**
- Altered tubular reabsorption of protein, glucose, amino acids and uric acid

**ELECTROLYTE BALANCE**
- Increased total body sodium up to 900–1,000 meq
- Increased total body potassium up to 320 meq
- Decrease in set point for thirst and ADH release
- Expansion of plasma volume
Renal function during pregnancy

Current literature:

• Creatinine falls in pregnancy and rises in 3rd trimester
• Creatinine falls by 35 μmol/L in pregnancy
• Average creatinine in pregnancy is 53 μmol/L
• Creatinine > 90 μmol/L = AKI
Arg + Glyc

Guanidinoacetate (or glycocyamine)

Creatinined
Generation of creatinine

Arg + Glyc

Guanidinoacetate (or glycocyamine)

Creatine

Arg + Glyc

Arg + Glyc
Generation of creatinine

- Arg + Glyc
- Guanidinoacetate (or glycocyamine)
- Creatine
- Systemic circulation

Arg + Glyc → Guanidinoacetate (or glycocyamine) → Creatine → Systemic circulation
Generation of creatinine

Arg + Glyc → creatine (in red meat) → systemic circulation

Arg + Glyc → guanidinoacetate (or glycocyamine)

Arg + Glyc → creatine
Generation of creatinine

- Arg + Glyc
- creatine (in red meat)
- systemic circulation
- creatinine
- guanidinoacetate (or glycocyamine)
- Arg + Glyc
- creatine → phosphocreatine
- creatine → creatinine
- Arg + Glyc
Generation of creatinine

**Creatine**
- (in red meat)

**Guanidinoacetate** (or glycyamine)

**Creatine**

**Clearance**
- glomerular filtration
- no tubular resorption
- some tubular secretion
Tubular secretion of creatinine

Elevated creatinine means: GFR < 50 mls/min!
Potential pitfalls of current AKI classifications
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### Consequence

- Reduced production of creatine; delayed diagnosis of AKI
- Mis-diagnosis of AKI
- Increased creatine availability (ie. red meat, creatine products)
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Many different criteria in literature:

- doubling of Screa
- Screa >70μmol/L
- 1.5x increase of Screa
- modified RIFLE or AKIN classification
- need for dialysis

Urgent need for consensus and better diagnostic tools
Renal problems during pregnancy

AKI in patients with normal renal function
  pregnancy related
  non-pregnancy related

AKI in patients with pre-existing renal disease
  “flare” of underlying renal disease
  acute on chronic kidney disease during critical illness
  AKI in renal transplant patients

CKD / ESRD patients
Variable incidence and mortality worldwide

Relevant factors: comorbid risk factors
definition of AKI
country
ICU vs non-ICU setting
access to prenatal care
access to abortion service
## Epidemiology of AKI during pregnancy

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<tr>
<th>Country</th>
<th>Cases of AKI</th>
<th>Hospital Mortality</th>
<th>Definition of AKI</th>
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<td><strong>Pakistan</strong></td>
<td>~10% of all cases</td>
<td>Fall from 18% to 7%</td>
<td>Crea &gt;1.5mg/dL + Urea &gt; 55mg/dL or 25% rise of creatinine and urea from baseline</td>
</tr>
<tr>
<td><strong>US</strong></td>
<td>4% of all cases</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td><strong>Italy</strong></td>
<td>1956 – 1994: Fall in incidence from 43% to 0.5%</td>
<td>Fall in mortality from 31% to &lt;1%</td>
<td></td>
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<tr>
<td><strong>Asia/ Africa</strong></td>
<td>Mortality rates 10 – 55%</td>
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UK

2007 – 2010

323,737 admissions to 203 adult, general critical care units

Of 142,692 (44%) female admissions:

874 (0.6%) pregnant on admission

3,922 (2.7%) recently pregnant
### Reasons for ICU admission during pregnancy

#### Non-obstetric reasons

- Respiratory 35%
- Pneumonia 20%
- Asthma 7%
- PE 2%
- Cardiovascular 7%
- Gastrointestinal 12%
- Genitourinary 8%
- pyelonephritis 3%
- DKA 3%
- Neurological 5%

#### Obstetric reasons

- Peri / post-partum haemorrhage 34%
- Pre-eclampsia 7%
- Ectopic 4%
Pregnancy related AKI

- Pregnancy
- Delivery
- Postpartum
- Week 4
- Week 8
- Week 12
- Week 16
- Week 20
- Week 24
- Week 28
- Week 32
- Week 36
- Week 40
- Week 44

Main causes of AKI in critically ill pregnant women:

- Septic abortion
- Haemorrhage
- Sepsis
- Critical illness
- HELLP syndrome
- Pre-eclampsia/eclampsia
- Acute fatty liver
- Thrombotic microangiopathy/HUS
- Acute flare of underlying chronic renal disease
Pregnancy related AKI

Pre-eclampsia  ELLP  HELLP  AFLP  HUS / TTP
Common reason for admission to ICU

Pyelonephritis most common type of sepsis and AKI

Reduced incidence of septic abortion
Bilateral cortical necrosis due to severe hypoperfusion and/or DIC

Common causes:  
- septic abortion  
- placenta previa  
- abruptio placentae
Renal causes

1. Flare of underlying renal disease, ie. SLE
2. First presentation of renal disease
Change in attitude over last 3 decades – from contraindication to cautious optimism

<table>
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<th>CKD with serum creatinine (μmol/l)</th>
<th>Problems during pregnancy</th>
<th>Risk of progression to ESRD</th>
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<tbody>
<tr>
<td>&lt;120</td>
<td>26%</td>
<td>~6%</td>
</tr>
<tr>
<td>120-150</td>
<td>47%</td>
<td>20%</td>
</tr>
<tr>
<td>&gt;250</td>
<td>86%</td>
<td>53%</td>
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Fertility improves after transplantation

2-5% of women of childbearing age with renal transplant will become pregnant (up to 50% rate of unplanned pregnancies)
Fertility improves after transplantation

2-5% of women of childbearing age with renal transplant will become pregnant (up to 50% rate of unplanned pregnancies)

Special aspects:

- higher risk of hypertension during pregnancy
- higher risk of pre-eclampsia (~1/3)
- risk of ureteric obstruction from gravid uterus
- increased risk of UTIs
- need for close collaboration with transplant team
Management of AKI during pregnancy

Depends on aetiology of AKI

General measures:
- correction of fluid depletion
- correction of hypo- and hypertension
- avoidance of further renal insults
- adjustment of drugs

Avoid giving too much fluid
Depends on aetiology of AKI

General measures:
- correction of fluid depletion
- correction of hypo- and hypertension
- avoidance of further renal insults
- adjustment of drugs

Avoid giving too much fluid
Effects of fluid overload

Hypervolaemia

Cardiac congestion
- ventricular dilation
- release of cardiac enzymes
- impaired function

Renal congestion
- intra-renal congestion
- intra-renal hydrostatic pressure
- intratubular pressure
Renal biopsy to be considered in case of primary renal disease especially if AKI occurs before 24 weeks of gestation (slightly increased risk of bleeding ~1.6 - 4.4%)

Early delivery of fetus to be considered
Renal replacement therapy

- maternal or fetal indications

- better fetal outcomes with better control of uraemia (serum urea <18mmol/L)

- high risk of spontaneous miscarriage (~50%), premature labour and smaller babies
Choice of RRT

- IHD
- SLED PIRRT
- PD
- CRRT

Types:
- intermittent
- continuous
Choice of RRT

Clearance per hour:
- IHD: +++
- SLED PIRRT: ++
- CRRT: +

Fluid status:
- Intermittent
- Continuous

Fluctuations in urea/NH$_3$/Na$^+$:
Choice of RRT and effects on uraemic toxins

The graph illustrates the changes in BUN (mg/dL) over time (day) for different renal replacement therapies (RRT) such as CVVH, IHD, and SLED. The Y-axis represents BUN levels ranging from 0 to 120 mg/dL, while the X-axis represents time in days from 0 to 7.

- CVVH (dotted line) shows a relatively stable trend with slight fluctuations.
- IHD (red line) exhibits a periodic increase and decrease, suggesting a repetitive cleansing effect.
- SLED (green line) follows a similar pattern to IHD but with smaller oscillations.

The graph highlights the varying effectiveness of these therapies in managing uraemic toxins.
CRRT allows gentler fluid removal and avoids major fluctuations in metabolic parameters and fluid status.
Long-term effects of AKI
Long-term effects of AKI

Preeclampsia, Pregnancy, and Hypertension

Risk of Preeclampsia and Pregnancy Complications in Women With a History of Acute Kidney Injury

Jessica Sheehan Tangren, Wan Ahmad Hafiz Wan Md Adnan, Camille E. Powe, Jeffrey Ecker, Kate Bramham, Michelle A. Hladunewich, Elizabeth Ankers, S. Ananth Karumanchi, Ravi Thadhani

Retrospective review of women who delivered infants between 1998 - 2016

Analysis of 14 486 women

246 had previous AKI and with full recovery of renal function
Long-term effects of AKI

Association for All r-AKI

- Preeclampsia
- Cesarean Section
- Preterm Delivery
- SGA
- NICU Admission
- Composite Neonatal Outcome

Adjusted Odds Ratio

Hypertension 2018;72:451-459
Conclusions

No consensus definition of pregnancy-related AKI
BUT: any serum creatinine rise during pregnancy is abnormal.

There are specific pregnancy-related and non-pregnancy related causes of AKI.

Management consists of optimisation of haemodynamic and fluid status and avoidance of further nephrotoxins.

Indications for RRT include fetal aspects.

There is an urgent need for better markers of renal function during pregnancy and a consensus definition of AKI.