Acute Kidney Injury

In Neonates

Dr Mona Aslam

Consultant Paediatrician PCH

Neonatal AKI (Acute Renal Failure)

- Definition
- Incidence
- Risk factors
- Morbidity/Mortality
- Bio markers
- Follow up

NICE CG169 Aug 2013

Promises to save thousands of lives and hundreds of millions of pounds each year.

- Affects one in six people who are admitted
- Completely preventable, can lead to death in one in four.

NOTHING ON NEONATES

Definition

- **Lack of consensus**
- Sudden and reversible increment in serum creatinine
- ? Need for dialysis
- In 2004 Acute Dialysis Quality Initiative- RIFLE
- Risk
  Injury
  Faliure
  Loss
  Endstage

Uses criteria of creatinine, urine output

Neonatal AKI – 50% non oliguric

AKIN- Acute Kidney Injury Network revised AKI

Smaller changes in serum creat . Time frame 48 hrs

KDIGO Divi ded into Stage 1 2 3 AKI based on urine output and rise in creat

Comparison between AKI classification system in adults, older children and newborns

	Creatinine criteria		Urine output criteria		
	RIFLE	pRIFLE and nRIFLE	RIFLE	pRIFLE	nRIFLE
Risk	Increased creatinine x1.5 or GFR decreases >25%	Increased creatinine x1.5 or GFR decreases >25%	UO ≤0.5 mL/kg/h × 6 h	UO ≤0.5 mL/kg/h × 8 h	UO <1.5 mL/kg/h for 24 h
Injury	Increased creatinine x2 or GFR decreases >50%	Increased creatinine x2 or GFR decreases >50%	UO ≤0.5 mL/kg/h × 12 h	UO ≤0.5 mL/kg/h × 16 h	UO <1.0 mL/kg/h for 24 h
Failure	Increased creatinine x3 or GFR decreases >75% or creatinine >4 mg/dL (acute rise of >4 mg/dL)	Increased creatinine x3 or GFR decreases >75% or GFR <35 mL/min/1.73 m^2	UO ≤0.3 mL/kg/h × 24 h or anuria × 12 h	UO ≤0.3 mL/kg/h × 24 h or anuria × 12 h	UO <0.7 mL/kg/h for 24 h or anuria for 12 h

Problem with using creatinine as a marker of Renal Injury

Ped Neph 2009 24: 265-274

Reflects the mother's creatinine

- Rises after 25-50% of kidney function has already been lost
- Different methods to monitor serum creatinine , Jaffe/ Enzyme
- At lower GFR serum creatinine is secreted
- Affected by medication and bilirubin

Creatinine

- D1 – mothers
- D2-7 rapid decline in term infants (GFR 10-20mls, 30-40 after first 2 wks)
- 1-2 month reaches nadir

- Preterms sometimes get an initial rise in the first few days , declines over 1-2 weeks rapidly reaches nadir 2- 3 months

Incidence AKI in Neonates

- DEPENDS ON DEFINITION
- Published studies estimate that the incidence of AKI in critically ill neonates is between
- 8% and 24% Askenazi (2012)
- 10% and 61% Andreoli SP (2004)

Risk factors in Neonates

- Immature kidneys
- Fluid losses
- Infection – sepsis
- Asphyxia

Low Birth Weight

Medications – nephrotoxic, aminoglycosides, indomethacin,frusemide,

BPD?- some interaction which occurs between the lung and the kidney

Lines UVC/UAC

Polycythaemia

Cardiac surgery

Lack of Neonatal Studies

- Only few cases studied
- Asphyxia Gupta et al found a 47% incidence of AKI and 14.1% mortality in infants with Apgar scores ≤6
- LBW Koralkar et al. 2011 LBW infants <1,500 g
  18% of the VLBW infants developed AKI
  mortality rate 2.4 x greater than the others
- Post Cardiac surgery - Multicentred study 2012 64% had AKI CJ Morgan et al
- ECMO 80% and AKI was associated with an adjusted mortality rate that was 3.2 times higher (Ashkenazi – Paed Int Med 2011)
- Studies report over 50% of AKI cases to be non-oliguric –

Immature kidneys

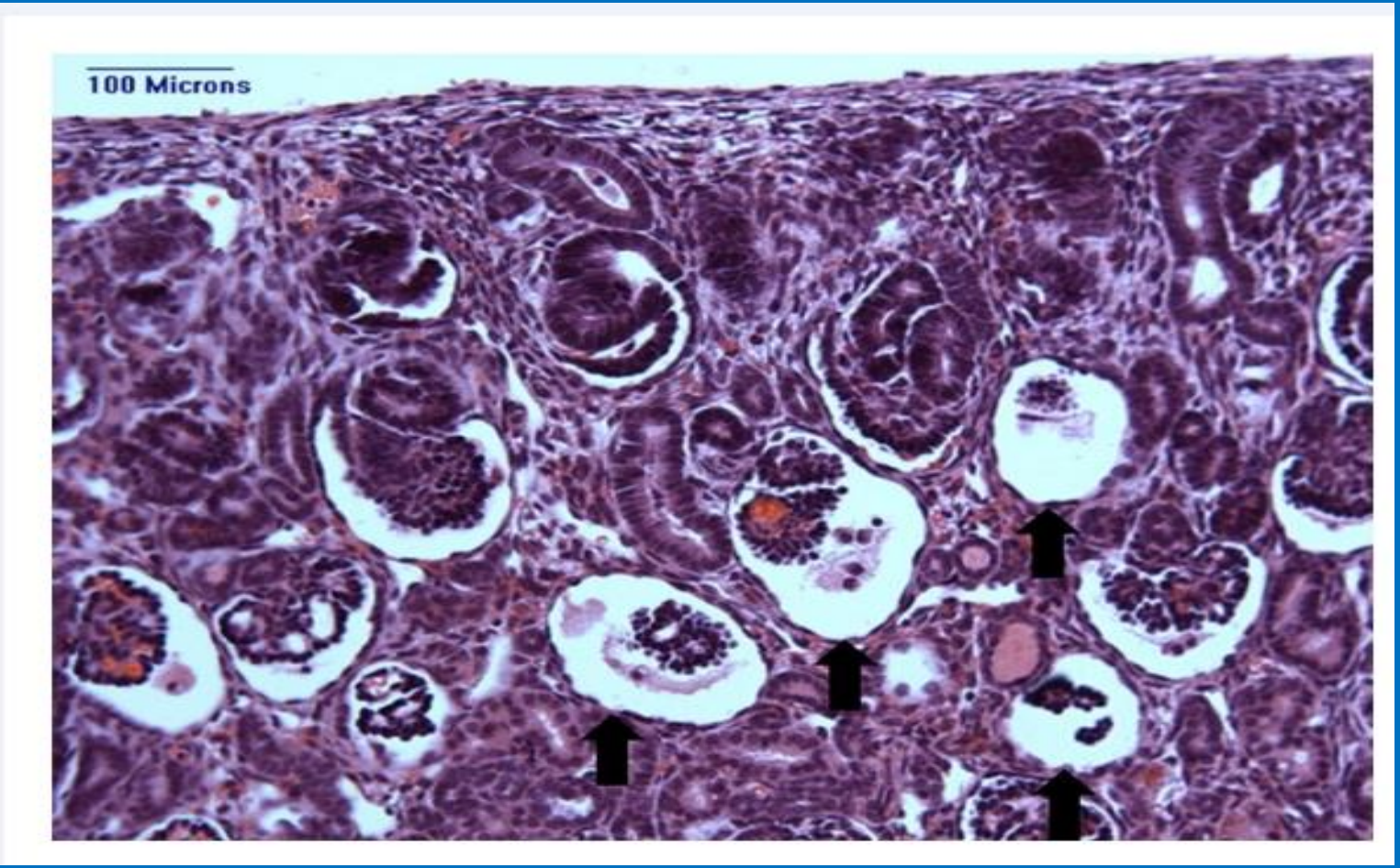
- Nephrogenesis - 8 to 34 weeks of gestn. 0.6-2 million nephrons
- Poor Nephronogenesis extrauterine life. Rodriguez et al (2004)measured number of glomeruli in autopsied specimens from prems . RGC in a straight line from cortex to capsule

1. Prems who died early had lower glomerular counts cf term babies

2. Prems who survived to term and then died also had fewer RCG cf to term babies Neo – Glomeruloneogenesis is affected ex utero

3. Infants with AKI had lower RCG than those without AKI Neo- Glomeruloneogensis is further affected by AKI

International journal of Nephrology – total nephron number the same but many glomeruli are abnormal. Glomeruli more cystic morphology



Low nephron mass leads to CRF

- Fewer functional nephrons
- Single nephron has to hypertrophy
- Hypertrophy causes increased capillary hydraulic pressure which causes capillary leak and glomerulosclerosis
- Proteinuria
- Hypertension
- Chronic kidney disease.

AKI in neonates
Why is it important?

- **Common** - Especially in Prems /VLBW
- **High Morbidity** - Long term effects - CKD / proteinuria/hypertension
- **High Mortality** - 8-36% of neonates with AKI

Biomarkers

- Current markers of AKI (GFR (creat) and urine output)
- Biomarkers signal injury early in the disease process intervene in the disease process at the onset of acute kidney 'injury' as opposed to attempting to fix acute kidney 'failure'
- NGAL, IL-18, Cystatin C, KIM
- B2 microglobulin, angotensinogen

Problems with Biomarkers

- Compared to creatinine
- Depends on gestational age
- Biomarkers are usually proteins released in injury rather of the nephron than markers of reduced GFR

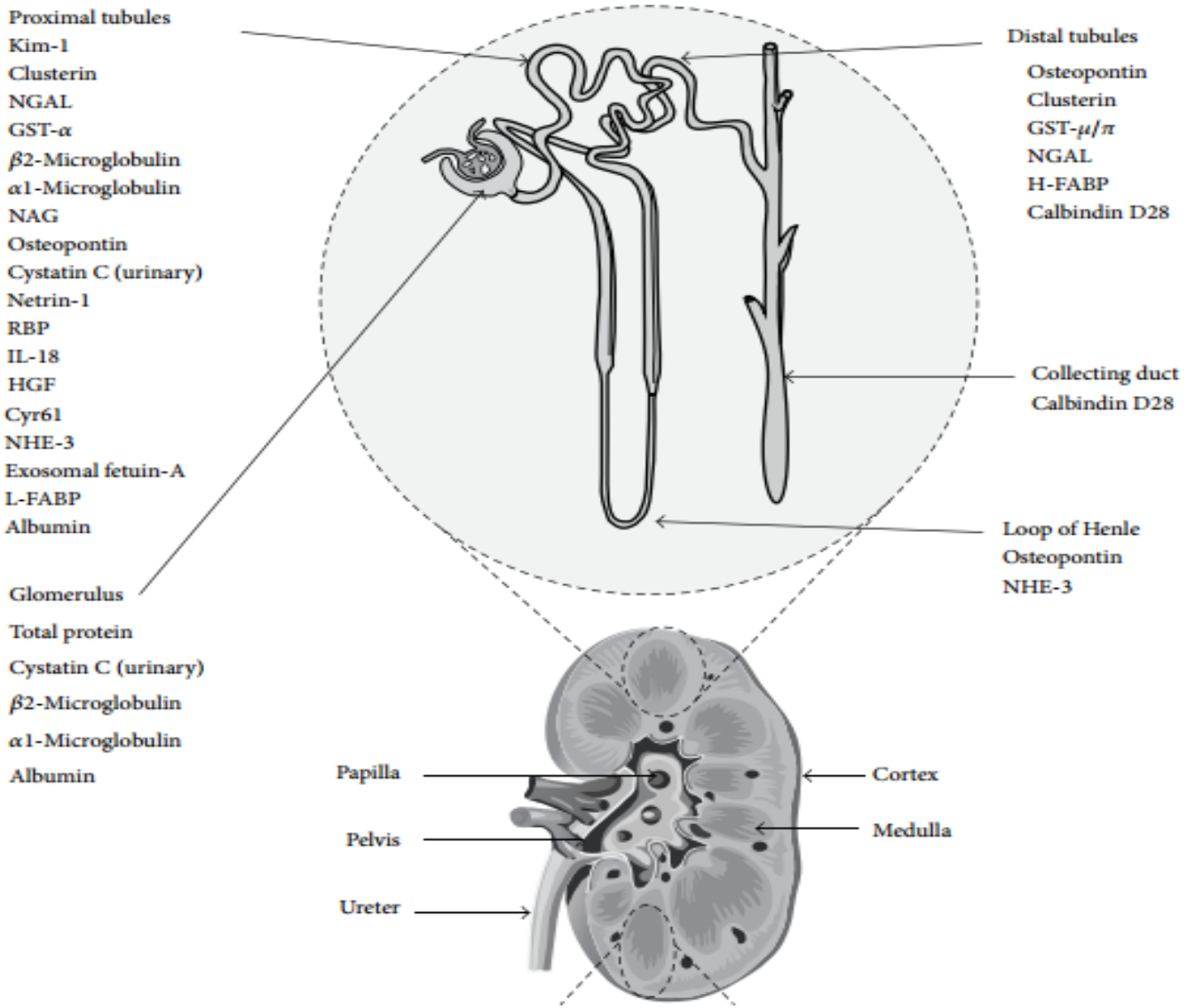


FIGURE 1: Nephron segment-specific biomarkers of kidney injury. Adapted from [40] with permission.

Biomarkers

- NGAL- neutrophil gelatinase associated lipocalin.
- Protein
- Expressed in the serum and the urine after ischaemia and AKI is upregulated and expressed protein in the kidney after ischaemia
- Has been measured in the neonatal population 2 hrs after CPB sensitivity and specificity 90%
- Also elevated baseline levels in prems and low birth weight babies- Lavery et al (2008)

Cystatin C

- Produced from nucleated cells it is a cystein proteinase inhibitor. Cleared exclusively by the kidney.

- Doesn't cross placenta
- Affected by tubular maturation

- RDS in preterm
- neonates with RDS, increasing before SCr [Pediatric Nephrology, 2013. Vol.28 (3), 477–484]

IL-18

- Proinflammatory cytokine, released in the proximal tubule after AKI
- Adults – urine levels elevated in ischaemic AKI
- Neonates following cardiopulmonary bypass
- Can be affected by sepsis

AKI ⟹ .....?CKD

- Most survivors of AKI have improved glomerular and tubular function at discharge
- After paediatric AKI, the mortality rate is high in the years after hospital discharge. In addition, over 50% of children have at least one sign of CKD 3–5 years after the initial event
- The exact incidence of CKD after AKI in neonates is unknown

Long term follow up of Extremely low birth weight infants with neonatal renal failure Miami Carolyn et al Paed Nephrology 2003

- Jan 1991- Dec 2001
- Ex LBW <1000g who had renal failure on NICU
- 18 yrs follow up
- Compared those with progressive renal disease at follow up Vs those with normal renal function
- Excluded those with a congenital renal abnormality.

Diagnosis

- The diagnosis of renal failure was made on the basis of a sustained increase in peak serum creatinine (SCr) >2.0 mg/dl (176.8 µmol/l)
- >48 h and/or oliguria (<0.5 ml/kg per hour urine flow for >24 h) during the neonatal course after the 3rd day of life

- 1yrs – est GFR Schwartz
- CRI if eGFR <75 ml/min/1.73m^2

- 12,608 infants admitted
- Overall mortality – 5%

- 1% had renal impairment (excluding congenital abnormalities/ infections) – mortality 46%
- <1000g Renal Failure mortality increased to 49% in those with renal failure
- 20 patients studied

- Current mean age is 7.5 ± 4.6 years (range 3.2–18.5 years)
- Birth weight averaged 686 ± 133 g (median 670 g)
- 9 patients showed a deterioration in function

	n GFR N=11	Low GFR <75 mls/min/1.73m² N=9	p=
age	5.7±2.2 (3-8.5)	9.9±5.6 (3-18)	P=0.03
Pk S Creat NICU	203±44.2 µmol/l	283±141 µmol/l),	P=0.08
1 year	35.4±8.8	79.6±27	P=0.001
Proteinuria on NICU	n=3	N=7	
Up/c mgs/mgs	1.4±0.8	5.8±0.8	P<0.0001
1 Year	0.5±0.3	4.9±4.0	P<0.01
BMI	64±33 percentile	91±14 percentile	P=0.03

Positive predictive values >75%

- Serum creatinine at 1 yr >0.6 mg/dl (53 µmol/l)
- Urine protein/creatinine at 1 year 0.6mg/mg

So which Neonates should be followed up?

- AKI +
- Especially if preterm
- Especially if VLBW
- Those who have significant proteinuria on discharge from NICU

When should they be seen ?

- At least at 1 year from a renal point of view- protein dipstick/ BP/Creat
- Refer to SPIN/Nephrologist if creat > 60 µmol/l urine protein/creat significant

- THANK YOU