ACUTE KIDNEY INJURY IN NEONATES

Thesis
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ABSTRACT

Acute kidney injury (AKI) is not just an innocent by-stander in the critically ill patient. Research on incidence and outcomes of AKI in the critically ill neonatal population is scarce. To date, observational studies suggest high rates of AKI and poor outcomes in critically ill neonates. Neonates with AKI are at risk of developing chronic kidney disease and hypertension.

Methods: 150 neonates were included in our study. They were classified into three groups. Group A: 50 neonates with risk factors and developed renal injury. Group B: 50 neonates with the same risk factors with normal kidney function. Group C: 50 neonates without risk factors and normal kidney function.

Objective: to know the association between AKI and the risk factors (sepsis, shock, perinatal asphyxia, congestive heart failure, mechanical ventilation, nephrotoxic drugs).

Results: Our study shows that shock was the main risk factor. Nephrotoxic drugs weren't associated with increased risk of developing AKI. CPAP has a protective effect on kidney function versus no ventilation or SIMV mode. Mortality rate was high in group A than group B. Neonates <36 wks gestation age showed a mortality rate higher than neonates $\geq$ 36 wk gestation age.

Key words: acute kidney injury, neonates

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LIST OF ABBREVIATIONS

ACE	: Angiotensin converting enzyme
AKI	: Acute kidney injury
BUN	: Blood urea nitrogen
Ca	: Calcium
CBC	: Complete blood count
CHF	: Congestive heart failure
CPAH	: Clearance of paraaminohippuric acid
CPAP	: Continuous positive airway pressure
Cr	: Creatinine
ECF	: Extracellular fluid
ERPE	: Effective renal plasma flow
FeNa	: Fractional excretion of sodium
GA	: Gestational age
GFR	: Glomerular filtration rate
GBM	: Glomerular basement membrane
HB	: Haemoglobin
HCT	: Haematocrit
K	: Potassium
Na	: Sodium
NEC	: Necrotizing enterocolites
PI	: Phosphate
Plt	: Platelet
PROM	: Premature rupture of membrane
RBF	: Renal blood flow
RPF	: Renal plasma flow
RVR	: Renal vascular resistance
SIMV	: Synchronized intermittent mandatory ventilation
SNGFR	: Single-nephron glomerular filtration rate
WBC's	: White blood cells

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INTRODUCTION

Acute kidney injury in the newborn is a common problem in the neonatal intensive care unit. The incidence of acute renal failure ranges from (6 – 24%) (***Andreali, 2002; Drukker, 2002***).

Acute kidney injury is commonly present among sick neonate. Asphyxia, respiratory distress syndrome, and urogenital anomalies are commonly reported causes of acute kidney injury in the west (***Mathur et al., 2006***).

In a full term neonate, the kidney functions are not fully mature and functional maturation continues in the postnatal age. Under normal circumstances, the kidneys adapt to various endogenous and exogenous stresses. However, in sick neonates and in stressfull conditions like sepsis and shock the adaptive capacities of the kidney may be overcome leading to renal dysfunction (***Jayashree et al., 1991***).

Acute renal failure carries poor prognosis and may even result in permanent renal damage in upto 40% of survivors (***Gupta et al., 2005***).

AIM OF THE WORK

To study the risk factors of acute kidney injury which include sepsis, shock, heart failure, premature rupture of membrane, necrotizing enterocolitis, nephrotoxic drugs, mechanical ventilation and prematurity and the outcome of these cases.

ANATOMY, EMBRYOLOGY AND FUNCTIONAL DEVELOPMENT OF THE KIDNEYS

EMBRYOLOGY OF THE KIDNEYS:

Potter (1972) has provided the most complete anatomic description human kidney development. Three sets of 'kidneys' form in mammalian embryos: the pronephros, mesonephros, and metanephros.

The metanephros is the direct precursor of the adult kidney, whereas the others essentially involute before birth ***(Woolf, 2008)***.

These three paired renal systems develop from the nephrogenic ridge of the mesoderm ***(Melanie and John, 2008)***.

Pronephros and mesonephros:

The first two systems, the pronephros and mesonephros, have limited function in the human being and are transient ***(Melanie and John, 2008)***.

In humans, the pronephros develops from the third embryonic week and contains rudimentary tubules opening into the pronephric duct The human mesonephros begins to develop in the fourth week of gestation and contains well-developed nephrons comprising vascularized gomeruli connected to proximal and distal-type tubules draining into the mesonephric duct, a continuation of the pronephric duct. The mesonephric duct extends to fuse with the cloaca, the urinary bladder precursor, at the end of the fourth week. The mesonephric tubules and duct form the efferent ductules of the epididymis, the vas deferens, the ejaculatory ducts and the seminal vesicles in the male. In the female they result in the vestigial, epoophoron and paroophron ***(Melanie and John, 2008)***.

Metanephrons:

The metanephrons represents the final development stage of the mammalian kidney. In humans, the metanephros appear 5 to 6 weeks after fertilization. It consists of two components which are the *ureteric bud epithelium*, a branch of the caudal mesonephric duct, and the *metanephric mesenchyme*. The ureteric bud and its branches form the epithelia of the collected ducts, renal pelvis, ureter and bladder trigone, whereas the metanephric mesenchyme differentiates into nephron tubules he interstitial fibroblasts ***(Risdon and Woolf, 1998)***.

The first metanephron glomeruli form by 9 weeks' and the final layer of nephrons forms by 36 weeks' gestation. The most mature nephrons are located; near the medulla, and the younger immature nephrons are found in. the outer cortex. Maturation proceeds after birth, but new nephrons are not formed in the human kidney. Kidney growth continues until adulthood mainly due to elongation of the proximal convoluted tubule and the loop of Henle and due to the growth of the interstitium ***(Tisher and Madsen, 1991)***.

There is evidence that nephrons in the developing metanephros may begin functioning as early as the 11^{tn} or 12^{tn} week after conception. Fetal urine is produced by the 12^{tn} week and its production increases with age until the end of pregnancy when urine makes up more than 60% of amount of amniotic fluid ***(Guignard and Drukker, 1998)***.

At inception of the metanephros, it receives its blood supply from the al sacral branches of the aorta. By 8 weeks' gestation, the metanephros is located in the lumbar position and ultimately the definitive renal arteries arise from the aorta at the level of the second jar vertebra ***(Risdon* and *Woolf, 1998)***.

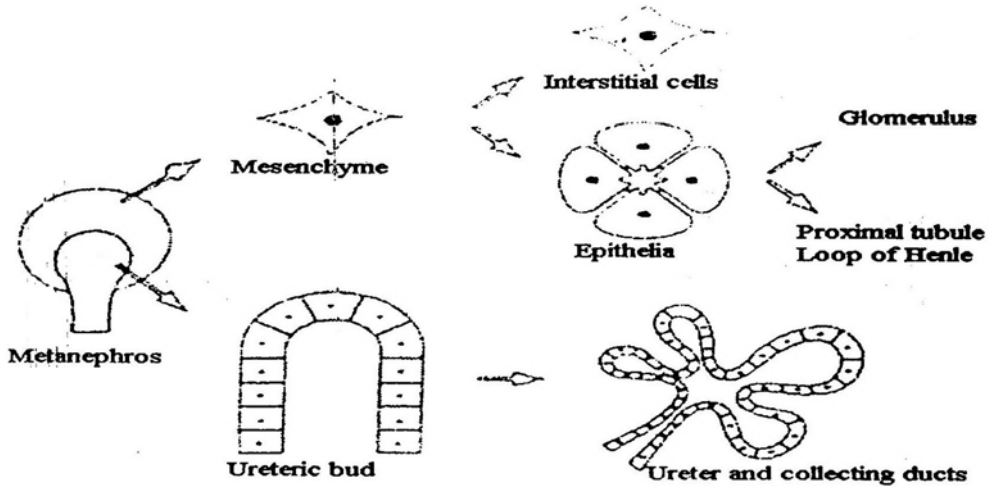

Figure 1: Main cell lineages arising in the metanephros

(Woolf, 2004).

ANATOMY OF THE KIDNEYS:

The kidney controls the composition and volume of body fluids within narrowly defined limits by excreting unwanted substances and regulating the excretion of essential metabolites. In addition, the kidney has other important roles, such as endocrine functions related particularly to blood volume, composition, and metabolic functions. It is a major site for degradation of compounds and an important source of production of essential metabolites. To fulfill these functions, the kidney has a unique structure ***(Field, et al., 1995)***.

The kidney lies in the retroperitoneal space slightly above the level of the umbilicus. They range in length and weight, respectively, from approximately 6 cm and 24 gm in a full-term newborn to 12 cm or more and 150 gm in an adult (***Ira and Ellis, 2007***).

Each kidney lies retroperiotoneally on the posterior abdominal wall in the para-ventral gutter from the 12^{th} thoracic to the 3^{rd} lumber vertebra. The right kidney is slightly lower than the left, reaching to about a finger breadth above the iliac crest. Its medial margin shows an indentation, called the renal hilum, at which are attached the renal artery, vein, lymphatics, nerves and the pelvic of the ureter (***Field, et al., 1995*)**

The kidney is closely surrounded by a fibrous capsule that normally strips easily from the surface. The fibroareolar tissue surrounding the kidney and the perinephric fat is condensed to form a sheath called renal fascia. The kidney is held in position partly through the attachments of the renal fascia, but principally by the apposition at the neighbouring viscera (***Ira and Ellis, 2007)***.

The cut surface of the kidney is subdivided into an outer pale layer **the cortex,** which contains the glomeruli, proximal and distal convoluted tubules, and collecting ducts, and an inner darker layer, the medulla, which contains the straight portions of the tubules, the loops of Henle, the vasa recta, and the terminal collecting ducts ***(Ira and Ellis, 2007)***.

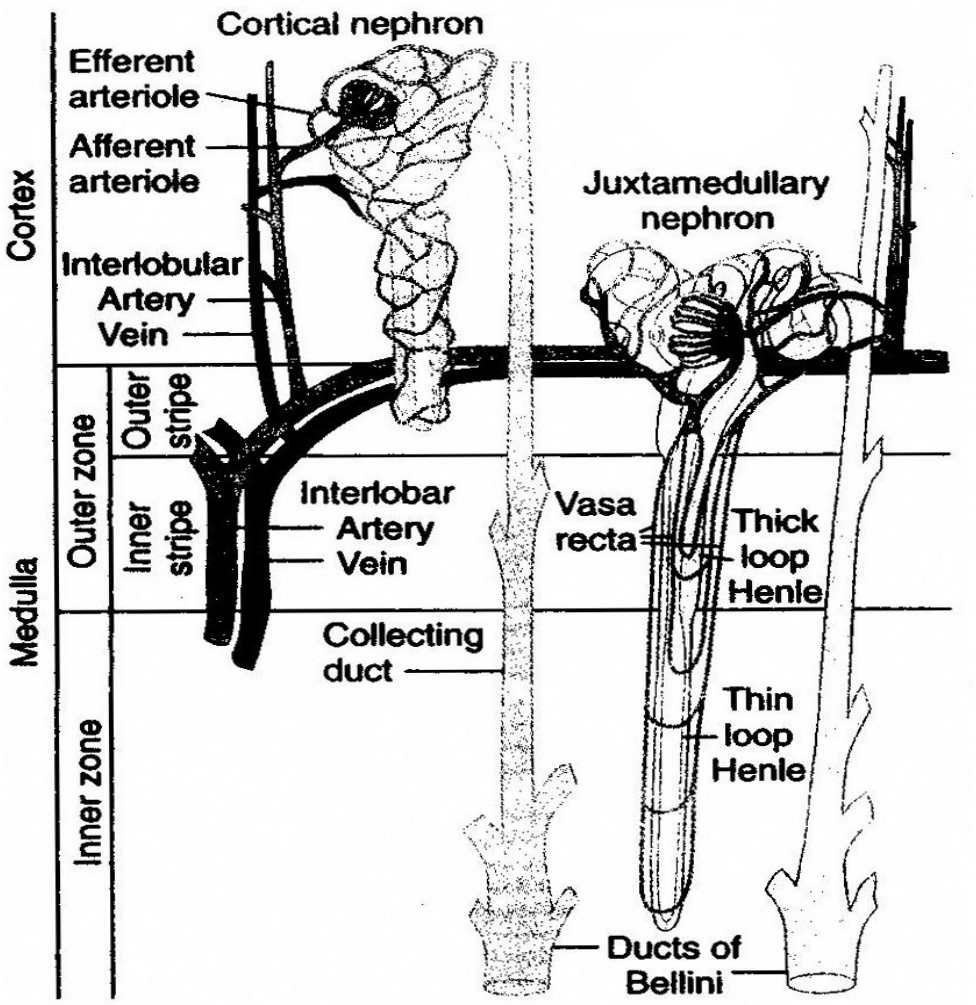

Figure 2: Comparison of the blood supplies of cortical and juxtamedullary nephrons.

(***Ira and Ellis, 2007***)

The nephron:

Each kidney contains approximately 1 million nephrons (glomeruli and associated tubules). In humans, formation of nephrons is complete at birth, but functional maturation with tubular growth and elongation continues during the first decade of life. Because new nephrons cannot be formed after birth, progressive loss of nephrons may lead to renal insufficiency. Decreased nephron number at birth may be associated with hypertension in adulthood, presumably related to hyperfiltration and "premature" sclerosis of overworked nephron units. This provocative hypothesis, if proven, could identify a major risk factor for hypertension and its associated cardiovascular complication in the newborn period (***Ira and Ellis, 2007***).

The first part of the nephron is the glomerulus, which is composed of a tuft of anastomosing capillaries projecting into the so called "Bowman's space". This space is enclosed by Bowman's capsule which is composed of: i) a basement membrane which is continuous with the basement membranes of the glomerular capillaries and the proximal tubules, and ii) the parietal epithelial cells which are continuous with the visceral epithelial cells ***(Ira and Ellis, 2007).***

The glomerular capillaries are supplied by an afferent arteriole and drained by a slightly smaller efferent arteriole. They are lined by endothelial cells which have thin cytoplasm characterized by the presence of multiple fenestrations (50-100nm in diameter).