

# **Causes and Risk factors of Acute Kidney Injury in Neonates**

Thesis submitted for the partial fulfillment of

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"أَمَّنْ هُوَ قَانَتْ آنَاءَ اللَّيْلِ سَاجِدًا  
وَقَائِمًا يَحْذَرُ الْآخِرَةَ وَيَرْجُو رَحْمَةً  
رَّبِّهِ قُلْ هَلْ يَسْتَوِي الَّذِينَ يَعْلَمُونَ  
وَالَّذِينَ لَا يَعْلَمُونَ إِنَّمَا يَتَذَكَّرُ أُولَٰؤُا  
الْأَلْبَاب"

سورة الزمر

الآية (9)

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## List of Abbreviations

<b>I.V</b>	Intravenous
<b>GBM</b>	Glomerular basement membrane
<b>RPP</b>	Renal perfusion pressure
<b>RVR</b>	Renal vascular resistance
<b>RBF</b>	Renal blood flow
<b>RPF</b>	Renal plasma flow
<b>ERPF</b>	Effective renal plasma flow
<b>CPAH</b>	Clearance of para-aminohippuric
<b>GFR</b>	Glomerular filtration rate
<b>NO</b>	Nitric oxide
<b>PTH</b>	Parathyroid hormone
<b>FeNa</b>	Fractional excretion of sodium
<b>ECF</b>	Extracellular fluid
<b>SNGFR</b>	Single-nephron glomerular filtration rate
<b>MW</b>	Molecular weight
<b>T<sub>mG</sub></b>	Maximum rate of glucose reabsorption

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# **Abstract**

Acute kidney injury is an independent risk factor for mortality in sick newborns. The aim of the current study was to evaluate the risk factors, etiology and outcome of cases of acute kidney injury, by using a retrospective study of neonates who were admitted at Cairo University hospital NICUS during the period of ( 2009-2011). The study revealed that the main risk factors for AKI are prematurity (39.7%), dehydration (36.5%) followed by sepsis (34.9%). Sixty three neonate out of 3042 neonates who fulfilled criteria of AKI. The main cause of death in AKI cases was combination of sepsis & dehydration (34%).

## **Key words**

Etiology Acute kidney injury neonates

## **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 %) (*Askenazi et al,2009*).

Acute kidney injury is commonly present among sick neonates. Asphyxia, respiratory distress, 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 stressful conditions, like sepsis and shock the adaptive capacities of the kidney may overcome leading to renal dysfunction

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

## **Aim of the work**

The aim of this study was to investigate the risk factors and causes for developing acute kidney injury in sick neonates admitted in neonatal intensive care units (NICUs) of EL Mounira Children Hospital and Gynecology and Obstetric Hospital, Cairo university during the period of 3 years (January 2009 - December 2011).

## EMBRYOLOGY OF THE KIDNEYS

**Potter (1972)** has provided the most complete anatomic description of 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, 2004**).

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 glomeruli 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 paroophoron (**Melanie and John, 2008**).

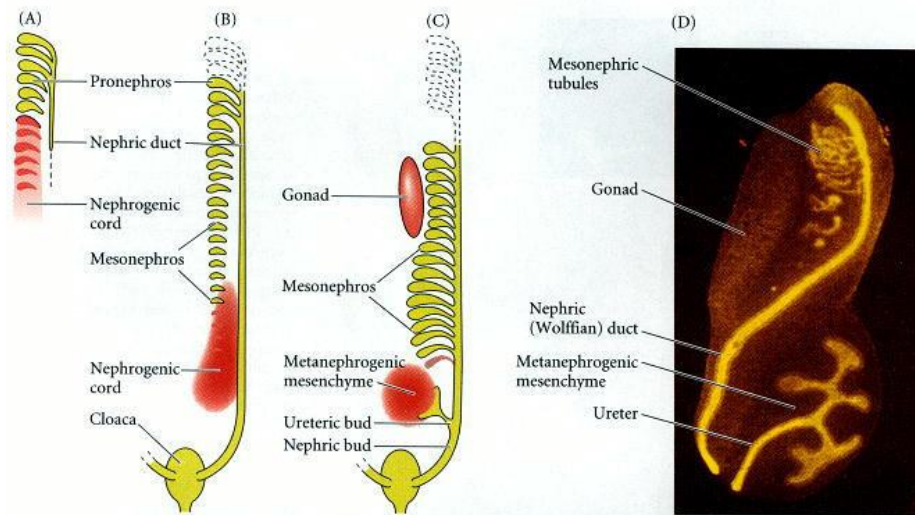
**Metanephrons:**

The metanephros represents the final development stage of the mammalian kidney. In humans, the metanephros appears 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 and the interstitial fibroblasts (*Risdon and Woolf, 2000*).

The first metanephric 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, 2001*).

There is evidence that nephrons in the developing metanephros may begin functioning as early as the 11<sup>th</sup> or 12<sup>th</sup> week after conception. Fetal urine is produced by the 12<sup>th</sup> week and its production increases with age until the end of pregnancy when urine makes up more than 60% of the amount of amniotic fluid (*Guignard and Drukker, 2009*).

At the inception of the metanephros, it receives its blood supply from the lateral 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 lumbar vertebra (*Risdon and Woolf, 2000*).



(Hill,2004)

Figure(1): Development stages of the human kidney :pronephros, mesonephros and metanephros.

## 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 and 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., 2004*).

The kidneys are two bean-shaped organs which lie slightly above the level of the umbilicus. They range in length and weight, respectively, from approximately 6 cm and 24 gm in full term newborn to 12 cm or more and 150 gm in the adult (*Davis and Avner, 2004*). Each kidney lies retroperitoneally on the posterior abdominal wall in the para-vertebral gutter from the 12<sup>th</sup> thoracic to the 3<sup>rd</sup> lumbar 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 pelvis of the ureter (*Field et al., 2004*).

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.

The cut surface of the kidney is subdivided into an outer pale layer, *the cortex*, which contains the glomeruli, proximal and distal convoluted