

ACUTE RENAL FAILURE AMONG INFANTS AND CHILDREN. INCIDENCE, CAUSES, MANAGEMENT, AND PROGNOSIS

THESIS

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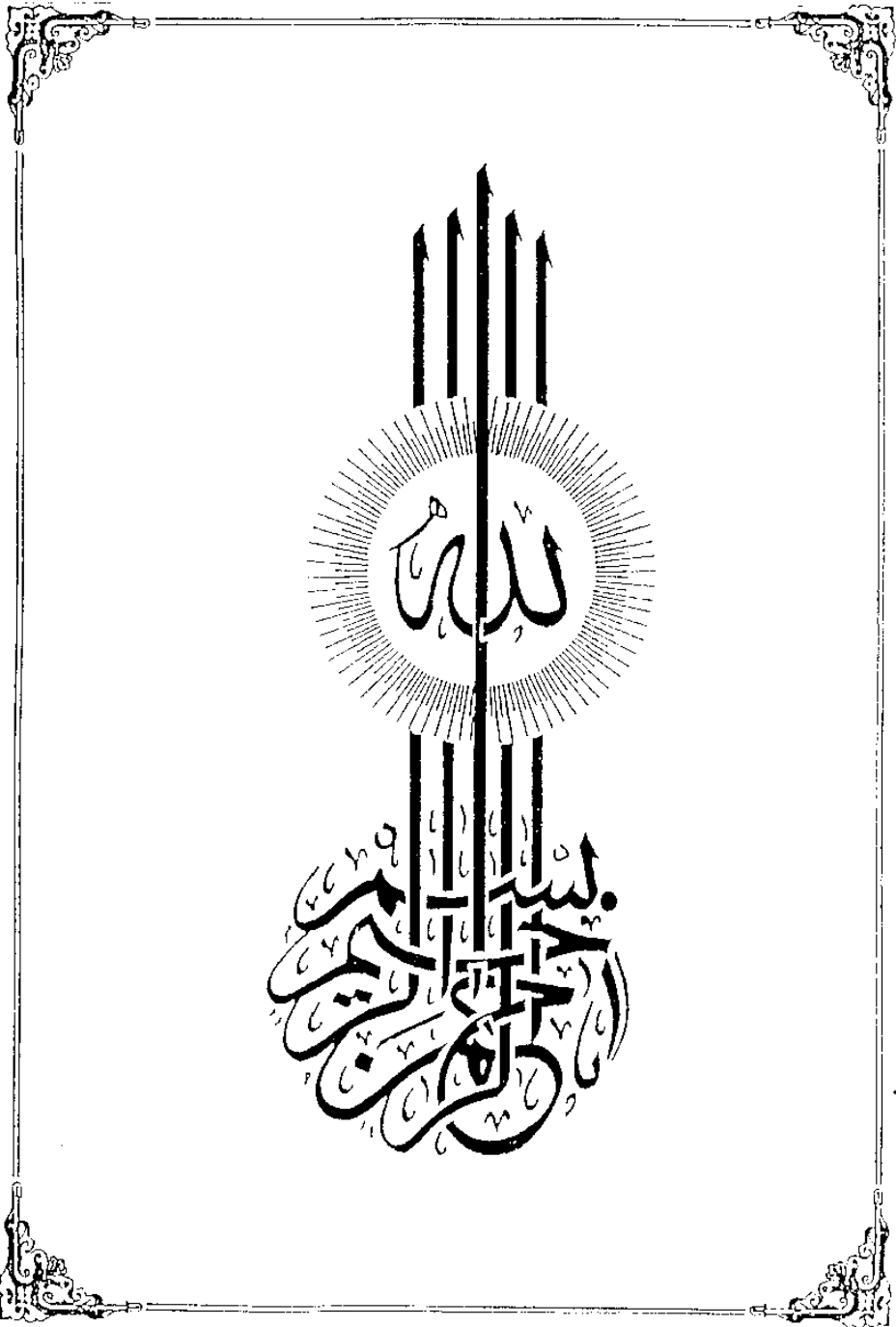
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**TO ALL THE SERIOUSLY ILL
AND DISABLED CHILDREN
OF OUR COUNTRY**



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INTRODUCTION AND AIM OF THE WORK

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Acute renal failure is defined as an abrupt decline in glomerular filtration rate sufficient in magnitude to result in retention of nitrogenous waste and disturbance of water and electrolyte balance (Arbus and Farine, 1986) (Feld et al., 1986) (Gaudio and Siegel, 1986) (Ikuma et al., 1988).

Acute renal failure occurs in infants and children due to a widely varied groups of diseases each of which is relatively uncommon (Groshong, 1980). The incidence and causes vary in different countries depending on health care, environmental conditions, and the age of the child or infant (Donckerwalke et al., 1983).

Acute renal failure in children was usually secondary to prerenal failure associated with gastroenteritis, sepsis etc. With improved understanding of fluid and electrolyte imbalance in paediatrics and the introduction of many new drugs, including antimicrobials, this has changed. Today, dose related nephrotoxic agents are a major factor in acute renal failure in many units and some drugs may cause acute interstitial nephritis which is not dose related (Arbus and Farine, 1986).

Other forms of therapy have also resulted in acute renal failure. For example, postoperative oliguria occurs in some patients after certain complex surgical procedures. In addition, diseases such as leukaemia may cause azotaemia in diverse ways (Arbus and Farine, 1986).

Although these newer factors in acute renal failure are important in major treatment centers, paediatricians will continue to see more traditional causes such as haemolytic uraemic syndrome and glomerulonephritis. In countries with warm climates, volume depletion remains the leading cause of acute renal failure in children. Postrenal azotaemia is rare, especially in children (Arbus and Farine, 1986).

There are functional limitations in the newborn kidney manifested by a higher blood urea and phosphate levels and a lower plasma bicarbonate concentrations. On the other hand, the functional demands on the infant's kidney are greater than on the adult kidney. This is because the metabolic rate of the infant related to body weight is considerably greater (Donckerwalke et al., 1983). Insensible water loss even at rest in a neutral thermal environment is five times greater, energy demands in relation to body weight about three times greater, and normal relative fluid intake about four times larger than in the adult. At least as important is the absence of normal thirst control in an individual who is unable to take more water when he is fluid depleted or sodium overloaded (Chantler, 1979). Therefore, it is not surprising that renal vascular causes of acute renal failure are especially prominent in the newborn, that dehydration leading to acute tubular necrosis is prevalent in infants, and that uraemia, acidosis and hyperkalaemia can develop with astonishing rapidity in a growing child (Thurau and Boylan, 1976) (Groshong, 1980) and (Donckerwalke et al., 1983)

Acute renal failure in infants and children carries a high mortality rate which reached up to 80% in the predialysis era (Segar et al., 1961). Dialysis has significantly improved the prognosis and lowered the mortality rate which may not exceed 4-10% in some centers (Gaudio and Siegel, 1987).

Aim of the work:

In this work, all infants and children suffering from acute renal failure during the last three years were evaluated and managed. The aim of this work was;

- 1] Identify the different causes of acute renal failure in infants and children
- 2] Identify the incidence of such causes in the development of acute renal failure, as well as pointing out the most common causes.

3] Evaluate the different lines of treatment for acute renal failure, as well as for specific diseases causing the renal derangement.

4] Find out the prognosis and final outcome of acute renal failure in such age group.

**REVIEW OF
LITERATURE**

CHAPTER I

DIAGNOSTIC CONSIDERATIONS

Successful management of acute renal failure in children and particularly infants, requires the knowledge of the functional characteristics of the kidney during development and an understanding of the metabolic balance of a growing child (Donckerwaile et al., 1983).

Development of the Kidney:

Renal development in the human starts taking place by the third to fifth week of gestation. Urine is first produced by the eleventh week. By the 34th week of gestation, nephrogenesis is complete. Most of the known renal homeostatic mechanisms are operative then in the foetus; although fluid and electrolyte regulation is accomplished almost entirely by the placenta. At the time of birth, the functional demands is placed entirely on the newborn kidney, whose performance will be largely dependent on the gestational age (Chevalier, 1986).

The new kidney is immature containing only 17% of its adult cellular compartment. At six months postnatally cellular division is complete and further growth is due to increase in cell size (Chantler, 1979). Nephron formation is complete before birth, but the superficial cortical nephrons are not functionally mature. Therefore, at birth the more mature juxtamedullary nephrons contribute to a greater proportion of the total glomerular filtration than in adults. This is associated with a proportional increase in juxtamedullary blood flow but total renal blood flow is small (Eldman, 1972).

Glomerular Filtration Rate:

At birth of term infants, glomerular filtration rate averages about 25 ml/min for every 1.73 square meter surface area. Rapid postnatal increase in blood flow is associated with a rapid increase in glomerular filtration rate to 48 ml/min at one month and to 80 ml/min at 6 months of age reaching

adult levels (corrected for body surface area) by the second year of life (Chevalier, 1986).

While glomerular filtration rate of term infants at birth is approximately 25 ml/min for every 1.73 square meter surface area, that of a premature baby is 10-20 ml/min. Glomerular filtration rate rises slowly, if at all, until reaching a conceptional age of 34 weeks, after which rapid increase in glomerular filtration rate is observed as in full term babies. This relates to the timing of completion of nephrogenesis at the 34th week (Chevalier, 1986).

Urea and Creatinine Handling:

While glomerular filtration rate reaches adult levels by the second year of life, the plasma creatinine and blood urea nitrogen do not reach adult values until 16-18 years of age (Moore et al., 1986). At birth, cord blood plasma creatinine has a mean level of 1.0mg/dl in the full term baby. By the second day, it falls to 0.9mg/dl to reach 0.6mg/dl at one week. The plasma creatinine values begin to reach normal paediatric levels of 0.3-1.1 mg% with a mean of 0.44mg/dl within 2-4 weeks of age (Chevalier, 1986). Thereafter, normal plasma creatinine concentration slowly increases with age and does not reach adult values until 16-18 years of age (Moore et al., 1986).

The same increments and decrements in relation to age is applied to the levels of blood urea nitrogen. In newborns and infants the blood urea nitrogen levels ranges 5-15mg% and in childhood the range is 10-20mg% (Moore et al., 1986).

Sodium Handling:

In the newborn kidney, fractional reabsorption of filtered sodium in the proximal tubule is reduced. However, the neonate is in a state of positive sodium balance which is a component of normal growth. This may be related to the enhanced sodium reabsorption by the distal tubules under the influence of circulating aldosterone, as well as decreased glomerular filtration rate. While term infants are capable of

sodium conservation during sodium deprivation, the infant with gestational age less than 35 weeks may develop negative sodium balance with resultant hyponatraemia. This tubuloglomerular imbalance may be due to immaturity and diminished tubular responsiveness to aldosterone. Therefore, it is recommended that such infants receive higher sodium intake (Chevalier, 1986). Normal fractional sodium excretion in the full term infant may be as high as 2-3% of the filtered sodium load compared to 1% of the older child or adult. Except in prematurely born infants, fractional sodium excretion generally reaches adult levels by the age of 2-4 months. In premature infants this may not occur before 4-6 months (Moore et al., 1986).

Potassium Handling:

The ability of the kidney to excrete potassium is less in the first month of life than later. Therefore, hyperkalaemia after this age is not a result of diminished renal excretory capacity for potassium (De Marchi et al., 1987).

Phosphorus and Calcium Handling:

Throughout the period of growth, urine phosphate excretion is low. Studies in both humans and animals showed a greater renal tubular phosphate reabsorptive capacity during growth compared to that in the adult (Moore et al., 1986). In a child tubular reabsorption of phosphate is almost 75-92% compared to 64-81% in the adult (Moore et al., 1986). At birth, serum inorganic phosphorus has a mean level of 6.05mg/dl, in an infant it reaches a mean level of 5.6mg/dl in the infant to a mean of 5.0 in a child reaching the normal mean of 3.65 in adulthood. Thus, normal plasma inorganic phosphate levels are higher in infants and young children than in adolescents. This fact is clinically important in the diagnosis, and treatment of renal failure in young children (Moore et al., 1986).

Some studies show that urine calcium excretion is low and renal tubular reabsorption of filtered calcium is high in the newborn period except in stressed infants or in very low birth weight infants (Arant et al., 1984).

Urine Concentrating Capacity:

Urine concentrating capacity is present beginning in utero. However, maximal concentrating capacity in early postnatal life is limited by protein intake and by additional physical factors such as kidney size. Postnatal ability to excrete a maximally dilute urine is quantitatively more developed than is the urinary concentrating capacity. Both processes reach adult levels within the first year of life. This is clinically important since the infant, particularly the immature infant, is more susceptible to dehydration and prerenal failure due to diminished urine concentrating capacity during periods of limited fluid intake or to vomiting and diarrhoea than to fluid overload when excessive intake occurs (Moore et al., 1986).

Acid-Base Handling:

The kidney participates in acid-base homeostasis through reabsorption of filtered bicarbonate and excretion of metabolic acid. These functions are present in utero but undergo major quantitative changes in postnatal life. Renal tubular reabsorption of filtered bicarbonate occurs mainly in the proximal tubule. The threshold of plasma bicarbonate concentration at which the filtered bicarbonate first appear in the urine is low in the newborn infant (19-21 mmol/l) and gradually increases to the adult value (24-26 mmol/l) by the age of four years. Normal values in the first four years of life reflect changes in the renal tubular bicarbonate threshold in this period. Therefore, normal plasma bicarbonate levels are lower in children than in adults (Moore et al., 1986).

Hydrogen ion excretion, which is primarily a distal tubular function, is lower in the neonate but there is no limitation to the ability of the infant to acidify the urine. Clinically; therefore, metabolic acidosis may result from the low glomerular filtration rate rather than the quantitative limitation in the hydrogen ion excretion. The quantitative capacity to excrete metabolic acid increases to the adult rate by the age of 12 months (Moore et al., 1986).

Handling of Other Solutes:

Renal tubular handling of glucose, amino acids, uric acid, chloride and magnesium also undergoes quantitative changes beginning in the newborn period. For example, fractional uric acid excretion in the newborn period is very high and declines to the adult range by one year of age. High fractional uric acid excretion in the newborn is manifested by the 'pink diaper' syndrome. Except perhaps for magnesium and uric acid, assessment of the renal handling of these solutes is mainly for purposes of diagnosis, rather than evaluation of renal function (Moore et al., 1986).

Functional Limitations of the Infant's and Child's Kidney:

There are functional limitations in the full term newborn kidney manifested by a higher blood urea and phosphate levels and a lower plasma bicarbonate concentrations. On the other hand, the functional demands on the newborn full term kidney are greater than on the adult kidney. This is because the metabolic rate of the infant related to body weight is considerably greater (Donckerwalke et al., 1983). Insensible water loss even at rest in a neutral thermal environment is five times greater, energy demands in relation to body weight about three times greater, and normal relative fluid intake about four times larger than in the adult. At least as important is the absence of normal thirst control in an individual who is unable to take more water when he is fluid depleted or sodium overloaded (Chantler, 1979). Therefore, it is not surprising that renal vascular causes of acute renal failure are especially prominent in the newborn, that dehydration leading to acute tubular necrosis is prevalent in infants, and that uraemia, acidosis and hyperkalaemia can develop with astonishing rapidity in a growing child (Thurau and Boylan, 1976) (Groshong, 1980) and (Donckerwalke et al., 1983).

Urine Output:

Under normal conditions, 28% of the cardiac output is distributed to the kidney (approximately 500 cc/min for each