EVALUATION OF SERUM CYSTATIN-C AS A NEW PARAMETER OF RENAL FUNCTION IN NEONATES

Thesis
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of Master Degree in ***Paediatrics***

By
Mahmoud Mohamed Mahmoud Zalam
M B B Ch

Supervised by
Prof Dr **Farida Ahmed Farid**
Professor of Paediatrics & Nephrology
Director of Paediatric Dialysis Unit
Ain Shams University

Dr **Ihab Zaki El-Hakim**
Lecturer in Paediatrics
Ain Shams University

Dr **Mona Mostafa Osman**
Lecturer in Clinical Pathology
Ain Shams University

Faculty of Medicine
Ain Shams University
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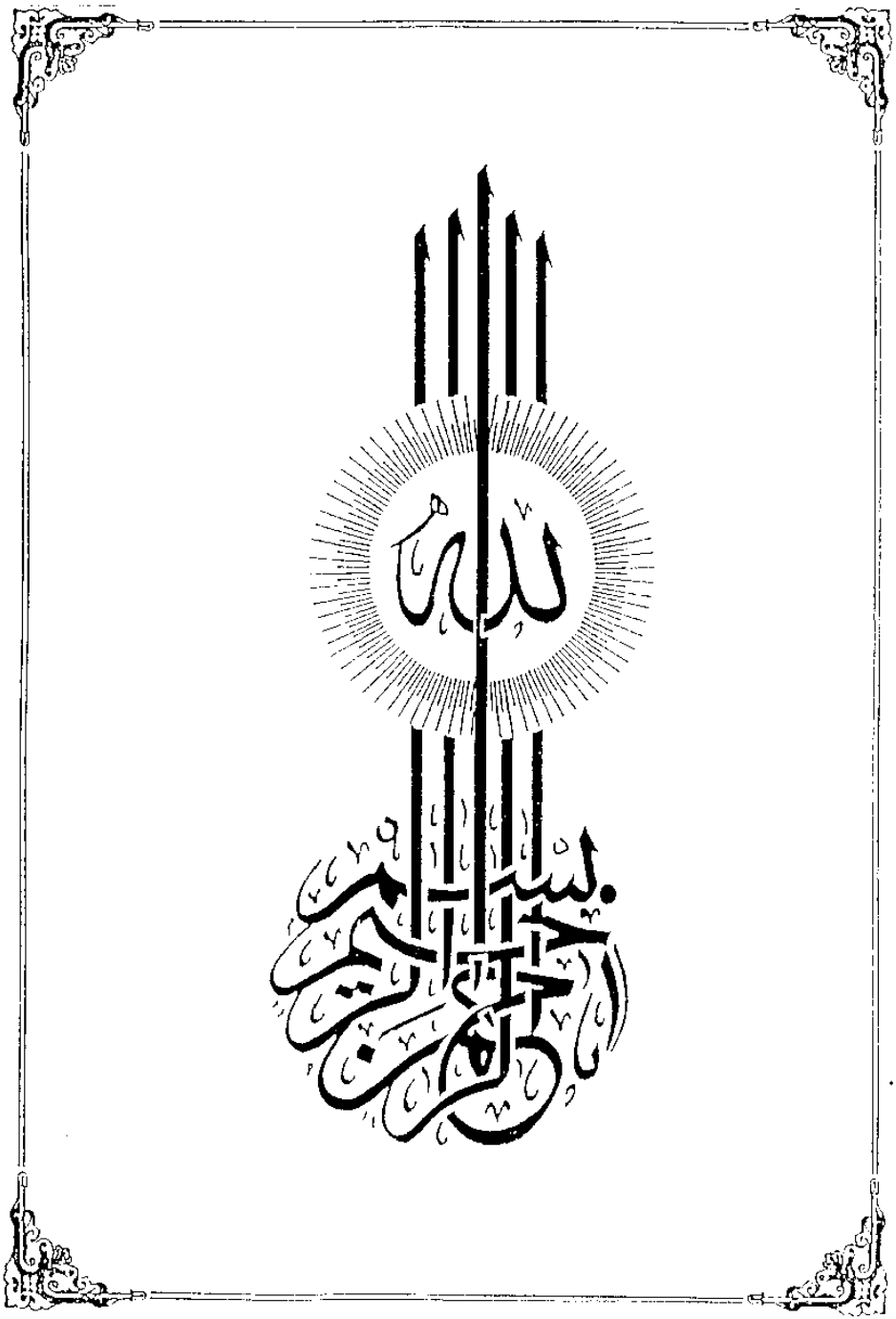

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LIST OF ABBREVIATIONS

A	Adenine
AD	Alzheimers disease
Arg	Arginine
AUC	Area under curve
AVP	Arginine vasopressin
BUN	Blood urea nitrogen
C	Cytosine
Cr	Creatinine
CRP	C- reactive protein
CSF	Cerebrospinal fluid
Cyst	Cystatin C
DIC	dissiminated intravascular coagulopathy
ECF	Extracellular fluid
ELISA	Enzyme linked immunosorbant assay
FE_{Na}	Fractional excretion of sodium
G	Guanine
GA	Gestational age
GFR	Glomerular filtration rate
Gly	Glycine
HCCAA	Heriditary cystatin C amyloid angiopathy
HCHWAD	Heriditary cerebral hemorrhage with amyloidosis dutch type
K^+	Potassium
Kb	Kilobase pair
Kda	Kilo dalton
LBW	Low birth weight
LMW	Low molecular weight
Lu	Glutamine
Mg^{++}	Magnesium
Na^+	Sodium
PETIA	particle enhanced tubidimetric immuno-assay
PTH	parathyroid hormone

RDS	Respiratory distress syndrome
ROC	Receiver operating characteristic
RVR	Renal vascular resistance
T	Thyamine
TRP	Tubular reabsorption of phosphate
VLBW	Very low birth weight

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Studies in adults have shown cystatin-C to be a more sensitive marker of changes in GFR than serum creatinine ***(Newman et al., 1995)***, and the same results were obtained in children ***(Bökenkamp et al., 1998)***.

Aim of the Work

The aim of this work is to evaluate the use of serum cystatin-C as a new parameter of renal function in healthy full term neonates and to investigate its possible value as an early predictor of renal affection in neonatal sepsis

reaches a plateau up to the time of birth reflecting a parallel increase in kidney size and renal function. The development of renal blood flow appears to follow the same pattern ***(Brion et al., 1997)***

During fetal life, the outer cortical glomeruli are relatively under perfused compared to the inner cortical (juxtamedullary) glomeruli. Following birth renal perfusion to the superficial cortical nephrons rises compared with the deep glomeruli. These changes in intrarenal blood flow distribution parallel the changes in glomerular morphological and functional maturation ***(Bergestin, et al., 1996)***.

Neonatal renal physiology:

The newborn's kidney differs from that of the older child and adult in glomerular and tubular function. The adult number of nephrons is achieved by 34 to 35 weeks of gestation but the nephrons are shorter and less functionally mature. Alterations in renal function and fluid and electrolyte balance are hightened in preterm infants who have not yet achieved their full complement of nephrons. When evaluating postnatal renal function both gestational age and post birth age must be considered since postnatal renal maturation is more of post birth than gestational age, that is a preterm infant who is several weeks old may have

more mature renal function than a newborn term infant ***(Blackburn and Loper, 1992)***.

Transitional events:

During intrauterine life the placenta is the major organ of excretion, handling many functions that are normally performed by the lungs and kidneys. With birth the kidneys must rapidly take over control of fluids and electrolyte balance, excretion of metabolic wastes, and other renal functions. Activity of arginine vasopressin (AVP) and the renin-angiotensin system increases with birth, perhaps stimulated by catecholamines, prostaglandins, hypercarbia and kinin-kallikrein system ***(Siegel, 1982)***.

As a result blood pressure increases with peripheral vasoconstriction and redistribution of blood flow to the vital organs ***(Guignard and Gouyan, 1988; Pohjavuori, 1983)***. Activity of the renin angiotension system increases further during the first few days after birth. Transitional increase in GFR may occur during the first 2 hours after birth ***(Bell, and Oh, 1987; Stewart and Jose, 1985)***.

Postnatal renal maturation:

During gestation the placenta, among its multiple functions, acts as a hemodialyzer perfrectly adapted to the fetal needs. Clamping of the cord is the signal for a stricking

increase in renal function. Changes that seem to be responsible for the rapid maturation of renal functions are a decrease in renal vascular resistance, an increase in systemic blood pressure and the effective filtration pressure and an increase in glomerular permeability and filtering area the latter is probably the major factor. The first micturation occurs in the first 24 hours of life in 93% of neonates, and 99.4% within 48 hours ***(Brion et al., 1997)***

About 23% urinate for the first time in the delivery room, where this event may be missed or not recorded. The force and direction of the urine stream are as important in assessing the urinary system as is the time of first voiding. A delay in spontaneous voiding in the absence of renal anomalies is usually due to inadequate perfusion with correction of the intravascular compartment and temporary expansion of interstitial fluid volume ***(Moore and Glavez, 1972)***.

Delayed voiding may occur in infants whose mothers received magnesium sulfate prior to delivery. Side effects of magnesium sulfate in the newborn include neuromuscular blockade with hypotonia and urine retention ***(Gonzales, 1985)***.

Renal blood flow:

About 20 to 25% of cardiac output is directed to the kidneys in adult while in the fetus proportion of cardiac output distributed to the kidneys is much lower and varies with species studied. In human fetuses, this percentage has been estimated to be as low as 4%. In term infants, this value is about 6% and increases to 8% to 10% by the end of the first week of life ***(Jose et al., 1994)***.

The relatively lower renal blood flow characteristic in the human fetus and newborn is associated with high renal vascular resistance and low filtrration fraction comapred with older children and adult ***(Van de Bor, 1995)***. The renal blood flow velocity increases whereas renal vascular resistance decreases during the 1st day of life.

Renal vascualr resistance (RVR) is normally high in the fetus since renal function is not essential in utero except for amniotic fluid production, therefore a small percentage of cardiac output perfuses the kidney. The higher (RVR and low blood flow in preterm infant to the outer cortex of the kidney may be due to the predominance of sympathetic tone in these infants ***(Green, 1987)***.

Renal blood flow is affected by changes in tissue oxygenation and blood pressure. Hypoxaemia both in the