UNIVERSITY OF PORT HARCOURT

CHILDCARE BEYOND CURE: THE SEARCH FOR, AND VALUE OF URINE

An Inaugural Lecture

By

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ORDER OF PROCEEDINGS

2.45P.M. GUESTS ARE SEATED

3.00P.M. ACADEMIC PROCESSION BEGINS

The procession shall enter the Ebitimi Banigo Auditorium, University Park, and the Congregation shall stand as the procession enters the hall in the following order:

ACADEMIC OFFICER
PROFESSORS
DEANS OF FACULTIES/SCHOOL
DEAN, SCHOOL OF GRADUATE STUDIES
PROVOST, COLLEGE OF HEALTH SCIENCES
LECTURER
REGISTRAR
DEPUTY VICE-CHANCELLOR [ACADEMIC]
DEPUTY VICE-CHANCELLOR [ADMINISTRATION]
VICE CHANCELLOR

After the Vice-Chancellor has ascended the dais, the congregation shall remain standing for the University of Port Harcourt Anthem.
The congregation shall thereafter resume their seats.

THE VICE-CHANCELLOR'S OPENING REMARKS.

The Registrar shall rise, cap, invite the Vice-Chancellor to make his opening remarks and introduce the Lecturer.
The Lecturer shall remain standing during the Introduction.

THE INAUGURAL LECTURE

The Lecturer shall step on the rostrum, cap and deliver her Inaugural Lecture. After the lecture, she shall step towards the Vice-Chancellor, cap and deliver a copy of the Inaugural Lecture to the Vice-Chancellor and resume her seat. The Vice-Chancellor shall present the document to the Registrar.

CLOSING

The Registrar shall rise, cap and invite the Vice-Chancellor to make his Closing Remarks.

THE VICE-CHANCELLOR'S CLOSING REMARKS.

The Vice-Chancellor shall then rise, cap and make his Closing Remarks. The Congregation shall rise for the University of Port Harcourt Anthem and remain standing as the Academic [Honour] Procession retreats in the following order:

VICE CHANCELLOR
DEPUTY VICE-CHANCELLOR [ADMINISTRATION]
DEPUTY VICE-CHANCELLOR [ACADEMIC]
REGISTRAR
LECTURER
PROVOST, COLLEGE OF HEALTH SCIENCES
DEAN, SCHOOL OF GRADUATE STUDIES
DEANS OF FACULTIES/SCHOOL
PROFESSORS
ACADEMIC OFFICER

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- The Vice-Chancellor
- Previous Vice-Chancellors
- Deputy Vice-Chancellors (Admin and Academic)
- Previous Deputy Vice-Chancellors
- Members of the Governing Council
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- Cherished Friends and Guests
- Unique Students of UNIPORT
- Members of the Press
- Distinguished Ladies and Gentlemen.

DEDICATION

This lecture is dedicated to my loving father, **Late Sir Felix Ogbonna Nwankwo** who as an educationist taught me early in life the great culture of hard work, perseverance and studiousness. He ensured that my dream of being a medical doctor was fulfilled.

AND

To all children with kidney diseases, and to the families who have lost any child from kidney disease.

ACKNOWLEDGEMENTS

I wish to specially thank the Almighty God who has guided and protected me in all my endeavours, and has made this Inaugural Lecture possible at His own time. He is my sustainer and my source of strength. May His name alone be praised.

I thank my dear husband, HRM Engr. /Sir Ben Anochie and our lovely children Dumogo, Zel and Somto for their deep love, understanding and affection.

I acknowledge my wonderful parents late Sir Felix Nwankwo and Lady Comfort Nwankwo who taught me the importance of education and hard work very early in life. I sincerely thank my dear siblings Engr. Felix Nwankwo, Mrs Ogochukwu Moore and Mr Emeka Nwankwo and their spouses for their love and support. My special thanks go to my dear uncles, Engrs. C.O Okoye and Emeka Nwawka, and to my special aunties, Barr. Franca Nwawka and Mrs Ngozi Okonkwo. I appreciate my cousins, aunties and uncles especially Mr Emmanuel Nwankwo who have contributed to my development from childhood.

I wish to thank all my lecturers in the University of Benin, and the Consultants/ doctors at the University of Benin Teaching Hospital during my Medical student years. Professor Fidelis Njokanma deserves my special appreciation.

My very special gratitude goes to my academic mother Professor Felicia Eke and her husband Professor Ndu Eke. Professor Felicia Eke's insistence made it possible for my employment as a lecturer, and thereafter, her tutelage and mentorship made my elevation to a professor happen at a record time. Professor KEO Nkanginieme has been a great pillar during my residency training and further development in Paediatrics.

I'm grateful to all the members of the Department of Paediatrics, and the other consultants who played active part during my academic journey namely Professors R. Oruamabo, E.A.D Alikor, Augusta Eneh, Alice Nte, Nwadiuto Akani and Dr Wari-Toby. I acknowledge Professor A. Ihekwaba who was my Consultant in the Department of Medicine during my housemanship in 1990, and Dr N. Inimgba who got me into the residency programme.

My unreserved thanks go to Dr Augustina Okpere for her support and partnership in steering paediatric Nephrology in Nigeria, and for reading through and editing this manuscript.

I acknowledge all my special friends and classmates of 1989 in the University of Benin especially Dr Magdalene Ajani, Professors Chioma Unachukwu and Barbara Otaigbe, Drs Bibian Ofoegbu, Emuebie Dibigbo and Adesuwa Adesina.

Special thanks to Professor Enobong Ikpeme, Drs Francisca Ikimalo, Uche Onubogu, Petronilla Tabansi, Tochi Uchenwa, Martha Okorie, Dennis Okoye, Ginika Udegbunam, Chioma Ohanenye, Chris Obinabor & the Adult Nephrologists. I wish to also thank the Renal Nurses in the Haemodialysis Unit and the staff of MacArthur Clinical Skills Laboratory.

Great thanks to my colleagues who encouraged me to book a date for this inaugural especially Professors Chijioke Nwauche and Hakeem Fawehinmi, DVC Academics, among many others

Many thanks also to members of Nephrology Association of Nigeria (NAN), Paediatric Nephrology Association of Nigeria (PNAN),African Paediatric Nephrology Association(AFPNA), International Paediatric Nephrology Association (IPNA) and International Society of Nephrology (ISN) for enabling my achievements in Paediatric Nephrology.

I wish to thank the Faculties that have assisted us at our annual Interventional Nephrology Clinical Skills workshop namely Professors Malcolm Lewis (United Kingdom), Rick Kaskel (USA), Henrietta Okafor, Emeka Nwankwo, and Drs Mordi Muorah (United Kingdom), Nneka Okoronkwo, Chukwuemeka Agi, Emmanuel Ocheli, Christopher Obiorah, ADNS W.S Eneyo and CNO I.N Chinda etc.

My deep gratitude goes to Professor Joseph Ajienka, the immediate past Vice-Chancellor of the Unique Uniport for finding me appointable as a Professor of Paediatrics, and a Director of the World Class Clinical Skills Laboratory, the first of its kind in Africa. I appreciate the Vice-Chancellor Professor Ndowa E. S. Lale for giving me this opportunity.

The past Chief Medical Directors of University of Port Harcourt Teaching Hospital especially Dr Uriah Etawo, Professor Aaron Ojule and the present CMD, Professor Henry Ugboma, and the members of the Administration deserve special appreciation, for creating a conducive environment for my research works and their support of our Nephrology activities. I wish to appreciate the current and past Provosts of the College of Health Sciences, especially Professors C. Didia and Christie Mato, current and past Deans of the Faculty of Clinical Sciences for providing a friendly working environment.

I thank all my spiritual fathers especially Pastor Yemi Oyenubi, Pastor Vincent Ebirim and Reverend Torty Onoh and their families for their prayers and encouragements, and my home social group, the Nibo Sisters.

Finally, I wish to sincerely thank again Professors Ndu Eke, Felicia Eke & KEO Nkanginieme, for proof reading and editing my manuscript.

PREAMBLE

At my professorial interview in 2011, the then Vice Chancellor, Prof Joseph Ajienka, asked if I could deliver my inaugural lecture before the end of the year and in my enthusiasm I answered in the affirmative. I didn't realize how fast time could fly and it's already eight years gone. Today is the appointed time for this Inaugural lecture to the glory of God, and as stated in Ecclesiastes 3:1 (KJV) –"*To everything there is a season, A time for every purpose under the heaven"* I sincerely thank God for this opportunity.

This presentation is on a bodily fluid, urine, which though common, is of immense medical significance. It is therefore my privilege to deliver this lecture titled ***"Childcare beyond cure: The Search for, and Value of urine",*** hoping that without difficulty, I will carry the academic community and the entire public along as the word urine is familiar to all.

Urine commonly called "wee" or "pee" by children is a watery, typically yellowish clear fluid. It is one of the body's chief means of eliminating excess water and salt, and nitrogen compounds such as urea and other waste substances removed from the blood by the kidneys.

As Paediatric Nephrologists caring for children's kidney and its diseases, we are pre-occupied with children making urine with so much emphasis on its volume, frequency, colour and flow (in males). The word "SEARCH" in the title was chosen to reflect a conscious effort by health workers, parents and care givers to pay attention to the urine of their patients and children. The bible passage in Matthew 7 : 7-8 (KJV)*"Ask, and it shall be given you; seek, and ye shall find; knock, and it shall be opened unto you. For every one that asketh receiveth; and he that seeketh findeth-"* supports being proactive.

This lecture is an opportunity to share my research works in the field of Paediatric Nephrology. Being a paediatrician, my studies are limited to children. The Oxford dictionary defines a child as "a young human being below the age of puberty or below the legal age of maturity". The United Nations Convention on the Rights of the Child in 1989 defines a *child* as "a human being below the age of 18 years unless under the law applicable to the child, majority is attained earlier.[1] We therefore, consider any individual from birth till 18years as a child in this lecture.

My choice of Paediatric Nephrology

Mr Vice-Chancellor Sir, before I proceed with this lecture I will briefly mention why I specialized in Paediatric Nephrology. My interest in Nephrology was borne out of an emotional circumstance when a very close relation was diagnosed with acute renal failure in the early years of my residency training in Paediatrics in 1993. During that time, haemodialysis was available in only one center, **EKO hospital** in Lagos, Nigeria. For the first time, I came in contact with dialysis machine and the process of dialysis with so much enthusiasm and trepidation.

Following this encounter and the success of his treatment to the glory of God, I resolved to develop my knowledge, skill and practice in the sub-specialty of Nephrology in the University of Port Harcourt Teaching Hospital. I worked under the tutelage of a renowned Paediatric Nephrologist, Prof Felicia Eke, as a senior resident doctor in training and continued with her upon my appointment as a Lecturer 1 in the University of Port Harcourt in August 1999 till date, learning the language of urine.

After my earlier embrace with Paediatric Nephrology, I went for a one-month Observership programme in the Division of Nephrology in the Department of Pediatrics, University of

Miami, Florida, USA in 2004. I have continued to improve my knowledge and skills even after my elevation to a professor. I had a 3-month fellowship training each at the University of Wales Hospital, Cardiff in 2012 and at the Birmingham Children's Hospital, United Kingdom in 2016 with Dr Mordi Muorah, and more recently, in the Division of Paediatric Nephrology in Children's Hospital At Montefiore, New York, for one month in 2019, with Professor Rick Kaskel. The journey to Paediatric Nephrology has been interesting due to the solid foundation laid by my mentor Prof Felicia Eke, although not without some challenges and sacrifices.

ANATOMY AND PHYSIOLOGY OF URINE PRODUCTION

Kidneys are the organs in the urinary system involved in urine production.[2] The urinary system basically consists of two kidneys, each having a ureter joining it to the bladder where urine is stored and discharged through the urethra (Figure 1). The kidneys are located at the back of the abdomen (retroperitoneally), on either side of the vertebral column, extend from vertebral level T12 to L3, but the right kidney is slightly lower. They measure approximately 5cm in length at birth, growing to adult size of 11-12cm by late adolescence, and are usually the size of the individual's clinched fist. Most individuals are endowed with two kidneys but a few have only one kidney.

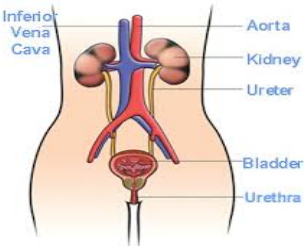


Figure 1: Urinary system (www.womens-health-advice.com).

Each kidney is composed of around 1 million functional units called **Nephrons**, which consist of renal corpuscles made of Bowman's capsule and glomerulus and its associated tubule, through which the glomerular filtrate passes before emerging as urine (Figure 2).

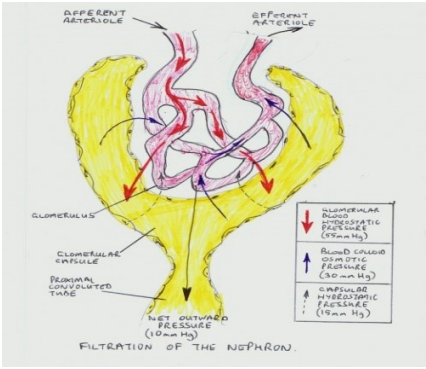


Figure 2: Renal corpuscle (www.wikiwand.com)

Majority of nephrons are subcortical while some are sub-juxtamedullary in location. Each nephron has its own supply of blood from two capillary regions from the renal artery. The kidneys receive 20% of the cardiac output, approximately 1liter/minute of blood flow.

The glomerulus is a capillary tuft that receives its blood supply from an afferent arteriole of the renal circulation. The glomerular blood pressure provides the driving force for water and solutes to be filtered out of the blood and into the space made by Bowman's capsule. The remainder of the blood passes into the efferent arteriole. The diameter of efferent arteriole is comparatively less than that of afferent arteriole, increasing the hydrostatic pressure in the glomerulus. It then moves into the vasa recta, which are only found in juxtamedullary nephrons and not cortical nephrons (Figure 3). The vasa recta are collecting capillaries intertwined with the loop of Henle through the interstitial space, in which the reabsorbed substances will also enter. This then combines with efferent venules from other nephrons into the renal vein, and rejoins the main blood stream.

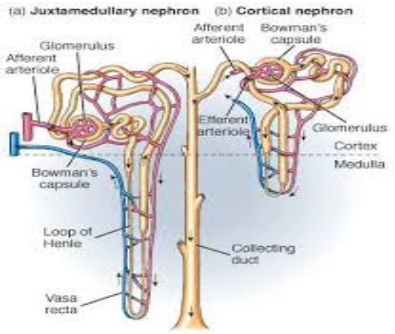


Figure 3: Juxtamedullary nephrons (www.sakshieducation.com)

The main process in the production of urine is that of simple ultra-filtration of the blood in the Bowman's capsule occurring between the semi- permeable walls of the glomerulus and the glomerular capsule. Glomerular filtration occurs when glomerular hydrostatic pressure exceeds the luminal hydrostatic pressure of Bowman’s capsule. The hydrostatic pressure of the glomerulus depends on systemic blood

pressure, autoregulatory mechanisms, sympathetic nervous activity, and paracrine hormones. [3]

There is also an opposing force, the osmotic pressure, which is typically higher in the glomerular capillary than in the Bowman's space because the filtration membrane limits the size of particles crossing the membrane. Certain substances such as water, mineral salts, amino acids, ketoacids, glucose, hormones, creatinine, urea, uric acid, toxins and certain drugs can be filtered while leukocytes, erythrocytes, platelets or plasma proteins cannot be filtered causing increase in osmotic pressure in the glomerular capillary.

Hydrostatic (fluid) pressure is sufficient to push water through the membrane despite the osmotic pressure working against it. The sum of all of the influences, both osmotic and hydrostatic, results in a net filtration pressure (NFP) of about 10 mm Hg.

After the filtration of fluid into the renal tubules, re-absorption and secretion of substances such as hydrogen ion, creatinine, and drugs occur from the blood through the peritubular capillary into the collecting tubule in order to produce urine. Approximately 65-70% of water, sodium and potassium, 100% glucose, bicarbonate, amino acids, citrate, and small peptides, 40-50% of calcium, and 80-95% of phosphate are reabsorbed from the tubular fluid into the blood stream so that only about 1–2 liters of urine are produced per day at a glomerular filtration rate of 100-125 mls/min.

The urine produced by the kidneys passes through the ureters and it's stored in the urinary bladder before being released to the exterior through the urethra.

DEVELOPMENT OF THE KIDNEY AND URINARY TRACT
Question- Do you know babies pee in the womb? Answer-Yes

Kidney development spans from 4 to 36 weeks gestational age (GA), although the point of completion can vary from 35 to 36 weeks (Figure 4). It develops from the intermediate mesoderm through 3 embryonic stages (pronephros, mesonephros and metanephros), until final development from ureteric bud and metanephric blastema.[4]

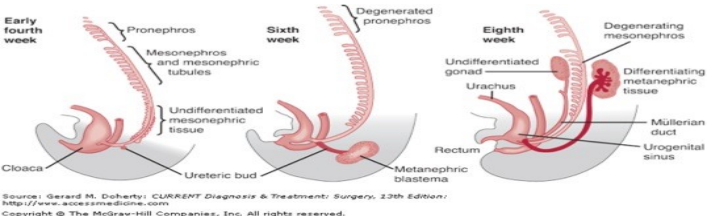


Figure 4: Foetal development of the urinary system (www. pediatricurologybook.com)

The ureteric bud forms the ureters, renal pelvis, calyces and collecting ducts while the metanephric blastema forms the nephrons and renal parenchyma (Figure 4b). It is important to note that nephron endowment is fixed for life since no new nephron is formed after 36 weeks GA.

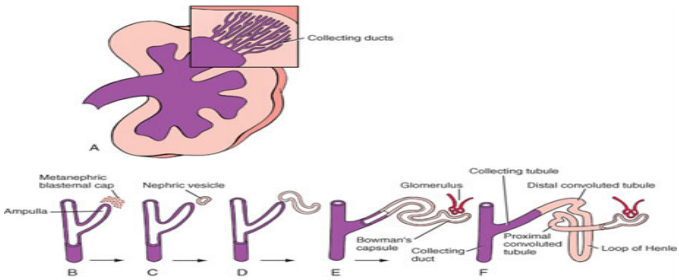


Figure 4b: Foetal development from the ureteric bud (www. pediatricurologybook.com).

The kidneys are formed in the pelvic region and they ascend into the final position at the upper part of the abdomen between the 6th and 9th week GA. The urogenital sinus develops into the urinary bladder and the urethra, with the female's urethra being shorter than the male's urethra.

The foetus begins to produce urine from the first trimester (10th to 12th week), which baby excretes into the amniotic fluid. The fetus breathes in and swallows some amniotic fluid which helps the baby to develop the ability to breathe and swallow.

Naturally, foetal urine isn't quite the same as yours or mine and the urine isn't yellow, either. Foetuses and newborns lack enzymes to convert bile pigments to urobilin, which colors the urine of older children and adults.

The development of the kidneys and urinary tract are influenced by genetic and environmental factors, thus maternal exposure to teratogens, angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARB), anti-seizure drugs and diseases such as diabetes mellitus affect normal development leading to congenital abnormalities of the kidneys and the urinary tract (CAKUT).[5,6]

MECHANISM OF MICTURITION

Physiology of Micturition

Micturition or Urination, also known as "wee-wee", "pee" or "piss" by most children in our environment, is the process or act of emptying urine from the urinary bladder through the urethra.[7] The process is regulated by nervous signals, both from the somatic and the autonomic nervous system (sympathetic and the parasympathetic nervous system).

Bladder storage and urination (micturition) involves complex interactions between the bladder, urethra, urethral sphincter, and the nervous system. The urinary bladder and urinary sphincters are the principal components of the lower urinary

tract (LUT) responsible for urinary storage and voiding. The urinary sphincters comprise of the internal urethral sphincters which are a continuation of detrusor smooth muscle that converges to form a thickened bladder neck and are under autonomic control (involuntary), and the external urethral sphincters which are folds of skeletal muscles formed when the urethral passes through the pelvic floor, and they are under somatic/voluntary control.

The storage of urine in the urinary bladder is initiated by the activation of stretch receptors in the bladder, which triggers spinal reflexes via the afferent nerves, resulting in stimulation of the sympathetic nerves, causing detrusor muscle relaxation, and contraction of the bladder neck (internal urinary sphincter). There is also voluntary contraction of the external urinary sphincter resulting in bladder filling (Figure 5).

The urinary bladder in children has a varying capacity which is determined using the Koff formula of 30(2+n) (where n is age in years) measured in milliliters, up to an average of 500mls in adolescents. [8]

Bladder emptying is initiated by stimulation of the stretch receptors in the distended bladder which results in activation of the micturition center in the pons, leading to parasympathetic motor neurons activation, with contraction of the detrusor muscle and relaxation of the urinary sphincters resulting in micturition (Figure 6).

Storage Reflexes

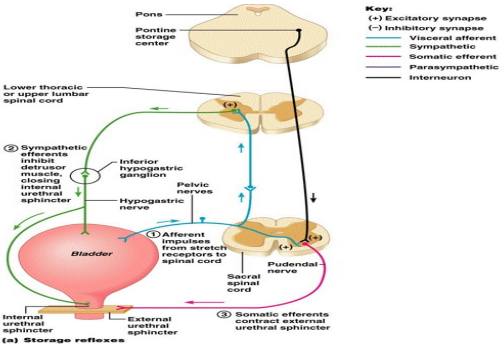


Figure 5-Sympathetic control of bladder storage (www.toppr.com/guides/biology/excretory products/micturition)

Micturition Reflex

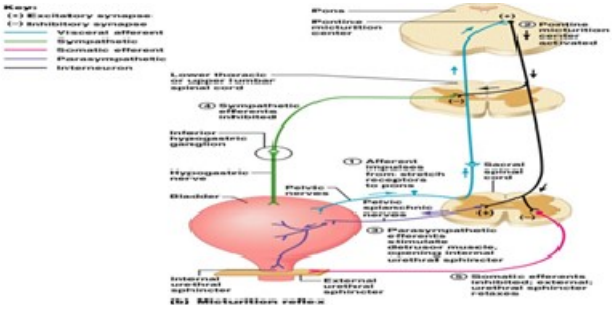


Figure 6- Micturition reflex (www.austincc.edu/apreview/Phys Text/ Renal.html)

In general, urinary bladder filling and storage is a function of the sympathetic nervous system, whereas micturition is a function of the parasympathetic nervous system. While both are autonomic functions in nature, the somatic nervous system is responsible for the control of the external urinary sphincter,

allowing for volitional continence. Voluntary control of the urinary sphincters depends on maturity of the nervous system which may lead to inhibition of purely involuntary micturition reflex until the time and place are appropriate (Figure 7). The ability to voluntarily inhibit micturition occurs by the age of 2 – 3 years, as control by higher levels of CNS develops. The complete control of the bladder during the night does not usually occur before 5 years of age.

Voluntary Control of Micturition

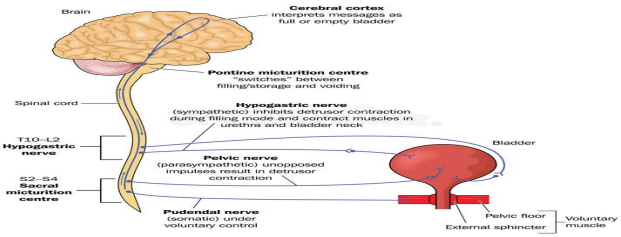


Figure 7- Voluntary control of micturition (www.der-querschnitt.de)

The normal frequency of urination varies widely in children. It depends on the age, diet, activity level, environment, bladder training, the state of hydration, or use of drugs such as diuretics.[9] Newborns void most frequently, because the bladder is small and the kidneys cannot concentrate urine. Daily urinary frequency typically decreases with age to an average of 4 to 8 times in a day as the child's bladder grows.

Urinary flow

Urinary flow is defined in terms of the size and force of the patient's stream. The caliber and force of the urinary stream vary greatly between individuals.[10,11] The normal urinary stream should be continuous for at least 80% of urination. Questions regarding the size and force of the urinary stream in

female patients are rarely fruitful unless extreme outlet obstruction is present.

The average urine flow rate varies according to age and sex.[11]For ages 4 to 7years, the average flow rate for both males and females is 10 ml/sec, while for ages 8 to 13years it is 12 ml/sec and 15ml/sec for males and females respectively, being higher in females due to their short urethra. The average flow rate for males at 14years and above is 21 ml/sec (Figure 8).

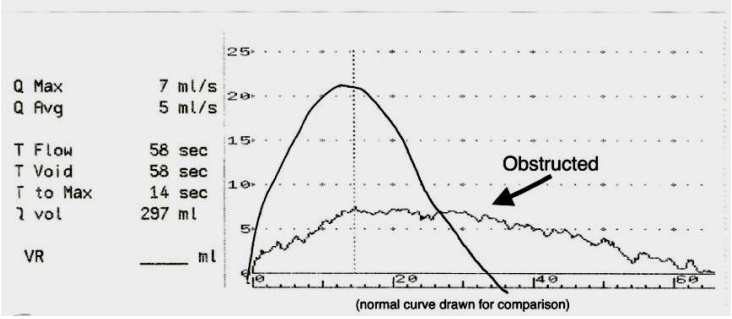


Figure 8: Normal urine flow rate curve (Continuous bell-shaped, smooth curve).
(www.centralmourology.com/procedure_types/uroflow)

The factors controlling the caliber of the urinary stream and the force of urinary flow are primarily mechanical, and secondarily influenced by volitional control. The force or pressure of the flow is initially generated by the bladder with some modification by the use of accessory abdominal muscles when the child is able to control urination. The caliber of the bladder outlet i.e. the bladder neck, posterior and anterior urethra, and the urethral meatus determine the force of urinary flow in males.

A brief history of Peeing Boy Statue-Manneken Pis.

Figure 9: Manneken Pis in Brussels.

This tiny peeing statue is an icon of Brussels, first mentioned in the archives dating back to 1452 **(**Figure 9). It is translated as "Little man Pee", depicting a naked boy urinating into a fountain. The statue of the "pissing boy," as he is commonly called, has led a long and not always easy life, surviving the bombardment of Brussels in 1695 and various wear and tear over the centuries. There are lots of stories behind this iconic statue; one tale maintains that the statue is a likeness of a boy named *Julianske* who saved Brussels from fire and disaster by peeing on the fuse of an explosive; another story depicts the boy as the victim of a witch's spell, frozen in time as punishment for peeing on her door.[12]

Mr Vice-Chancellor Sir, this national monument of Brussels is not only a tourist attraction site but an apt symbol of normal pee in males, thus important to the Nephrology community. I believe it was the good urinary stream of this boy which could "hit the wall" or "go across the bed" that enabled him put out fire with his urine and saved the entire city.

CHARACTERISTICS OF NORMAL URINE[3]

Urine is an incredibly complex bio-fluid, a by-product generated by cellular metabolism and cleared from the bloodstream by the kidneys.

According to researcher David Wishart, Professor of Biology and Computing Science at the University of Alberta, Canada "**We had no idea there could be so many different compounds going into our toilets"** This refers to the quality of the urine which is very essential in ensuring adequate clearance.

Composition- It is an aqueous solution of greater than 95% water, with the remaining constituents being nitrogenous waste substances. In the order of decreasing concentration the constituents are urea 9.3 g/l, chloride 1.87 g/l, sodium 1.17 g/l, potassium 0.750 g/l, creatinine 0.670 g/l, ammonia, uric acid and other dissolved ions, inorganic and organic compounds in trace quantities including small amount of proteins and hormones. About 80 percent of the dietary intake of nitrogen is balanced by the urinary excretion of nitrogenous compounds. The amount in the urine varies according to protein intake. Creatinine is an important nitrogenous compound in urine, and its level depends on the body mass and muscle mass, as well as age. The normal urine does not contain glucose, albumin, ketone bodies, nitrite, blood, microbes, white blood cells and bilirubin.

Colour- Urine varies in appearance, depending principally upon a body's level of hydration, as well as other factors such as drugs, natural chemicals from foods, and diseases. Normal urine is a clear transparent solution ranging from colourless to amber but is usually a pale yellow. In the urine of a healthy individual, the colour comes primarily from the presence of urobilin which is a final waste product resulting from the

breakdown of haeme from haemoglobin during the destruction of aging red blood cells.

Odour- In a healthy person urine is sterile until it reaches the urethra where epithelial cells lining the urethra are colonized by facultatively anaerobic Gram negative rods and cocci. The odour of human urine can reflect what has been consumed or specific diseases. However, normal urine does have a mild odour from the release of ammonia from the breakdown of urea.

pH - The kidney maintains the body's acid-base balance by excreting strong acids in the urine which is measured as the urine pH. The pH of urine can vary between 5 and 8, with a neutral of 7 in healthy individuals. Urine pH is a reflection of the body pH, and the lower the urine pH the greater the acidity. pH of urine can be affected by diet and some medical conditions. A diet high in citrus, vegetables can increase urine pH (alkaline) while a diet high in meat, protein and cranberry juice can decrease urine pH (more acidic). Too high or low urine pH can indicate the likelihood to form kidney stones. A low urine pH promotes formation of uric acid and cystine stones while high urine pH promotes calcium-phosphate precipitation.

Specific gravity- Urine specific gravity (SG) is a measure of concentration of the urine. Normal urine SG values vary between 1.010–1.035. Fluid intake and disease conditions can affect the concentrating ability of the kidneys and the urine SG. In a healthy individual, the urine SG reflects recent fluid intake. A high SG may reflect dehydration while a low SG indicates inability of the kidneys to appropriately concentrate urine.

Volume- The urine volume is the amount of urine produced by the kidneys. The average urine volume is dependent on the state of hydration, activity level, environmental factors, weight, and the individual's health. The normal urine output in neonate is 2-3mls/kg/hour, infant 2 mls/kg/hour, child 1-2 mls/kg/hour and adolescent 0.5-1 mls/kg/hour. Reduced urine volume is regarded as oliguria if urine output is <0.5mls/kg/hour in older children or <1ml/kg/hr in infants, and anuria if less than 1ml/kg/day or absence of any urine output. Excessive urine volume known as polyuria is urine output >4mls/kg/hour or > 2.5 L/day. A healthy newborn may not have urine output for 24 hours after birth.

THE VALUE OF URINE

The value of urine lies in its ability to remove the waste products of metabolism that are dangerous to body tissues and functions. Urine stands out in the wealth of information it grants about a patient's condition. It is valuable in quantity and quality as these characteristics reflect the state of health of the kidneys and the urinary tract.

Urine has been described as a "liquid gold". Please permit me to ask this great audience if there is anyone that has not passed urine today? This highlights the value of urine because **"We wee to live, and not live to wee, for whence we stop to wee, we start to die"** (Ifeoma Anochie 2019)**.**

According to Dr. Michael Farber, director of the Executive Health Program at Hackensack University Medical Center in Hackensack, New Jersey, the appearance and smell of your urine as well as the frequency with which you have to go and the flow of urine can provide many clues to what else is going on in your body**.**[13] **"What your urine is telling us about your health"** (Figure 10)**.**

Figure 10: Normal & Abnormal urine (www.healthtap.com)

Colourless urine indicates over-hydration (drinking too much), which is preferred to dehydration, though it can remove essential salts from the body. Dark yellow urine is often indicative of dehydration with concentrated urine, and yellow/light orange urine may be from presence of excess B-vitamins removed from the blood stream. Certain medications such as rifampicin and phenazopyridine can cause orange-red urine, and consumption of beets can change the urine to red or pink. In some disease conditions, urine may be coloured from body metabolites such as red (blood), dark orange to brown (bilirubin or myoglobin). Green urine may result from drinking highly colored beverages or from a urinary tract infection.

"By editing urine out of the bloodstream, kidneys preserve the primordial sea in our blood, maintaining the balance of salt essential to our survival" (Dr Jonathan Reisman, 2016).

OVERVIEW OF KIDNEY DISEASES AND MY CONTRIBUTIONS TO KNOWLEDGE

There are many kidney diseases that affect urine production, its characteristics and normal urination. I wish to discuss some of these diseases and share my research works as contributions to knowledge in the past 20years.

ACUTE KIDNEY INJURY (AKI)

Acute kidney injury (AKI) formerly known as acute renal failure is a sudden and rapid deterioration in kidney function which results in the accumulation of nitrogenous waste substances such as urea and creatinine which are harmful to the individual.[14]

Classification of AKI.

AKI has been conventionally classified into 3 categories based; on the anatomic location of the initial injury into pre-renal, intrinsic and post-renal; based on urine output into oliguric and non-oliguric; and according to circumstance in which AKI occurs as community-acquired AKI or hospital–acquired. Community acquired AKI is the common form seen in our environment and has a good prognosis if early intervention is provided. It is more likely associated with a single predominant insult, which are mostly preventable, while hospital-acquired AKI is seen especially in critical care setting, and the cause is frequently multifactorial. It is usually part of severe multi-organ failure.

Definitions

Several classification systems have been proposed to standardize the definition of AKI.[14,15-17] In May 2002, the Acute Dialysis Quality Initiative (ADQI) group for the study of AKI, composed of nephrologists and intensivists developed RIFLE (Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease) classification, to define and stratify the severity of AKI.[15] The RIFLE criteria depend on changes within 7days in the serum creatinine (SCr) or glomerular filtration rates and/or urine output. Paediatric modified RIFLE was developed to characterize the pattern of AKI in critically ill children (Table 1).

Table 1: pRIFLE CLASSIFICATION

CRITERIA	ESTIMATED CCL	URINE OUTPUT
Risk	eCCl decrease by 25%	<0.5mL/kg/hr for 8hr
Injury	eCCl decrease by 50%	<0.5mL/kg/hr for 16hr
Failure	eCCl decrease by 75% or eCCl <35mL/min/1.73m2	<0.3mL/kg/hr for 24hr Or anuric for 12hr
Loss	Persistent failure>4wk	
End-stage	End-stage renal disease (Persistent failure>3mo)	

The limitations of RIFLE criteria include its dependent on estimation of Glomerular filtration rate (GRF) which begins to decrease when there is considerable kidney damage, and therefore not a reliable marker in AKI. In March 2007, Acute Kidney Injury Network **(**AKIN) classification, a modified version of the RIFLE, was released.[16] It grouped AKI from mild to severe injury based on abrupt reduction in kidney function within 48hours, with absolute rise in SCr of ≥0.3mg/dl (≥26.4 µmol/L), or percentage increase of SCr of 50% (>1.5x) rise from baseline, and reduced urine output, without recourse to GFR. More recently in 2012, Kidney Disease Initiative Global Outcome (KDIGO) classified AKI using the two criteria as shown in Table 2.[17]

Table 2: KDIGO STAGING OF AKI

Staging of AKI(KDIGO)

Stage	Serum Creatinine	Urine output
1	1.5-1.9 times baseline within 1 wk or ≥ 0.3 mg/dl increase within 48 hrs	<0.5ml/kg/h for 6-12 hrs
2	2.0-2.9 times baseline	<0.5ml/kg/h for ≥ 12 hrs
3	3.0 times baseline or increase in serum creat to ≥ 4.0 mg/dl or initiation of RRT or in patients < 18 yrs, decrease in eGFR to <35ml/min per 1.73 m²)	<0.3ml/kg/h for ≥ 24 hrs or Anuria for ≥ 12 hrs

Pathogenesis and Causes of Acute Kidney Injury

Figure 11 shows the pathogenesis of AKI with pre-renal injury being the commonest mechanism of AKI in children.

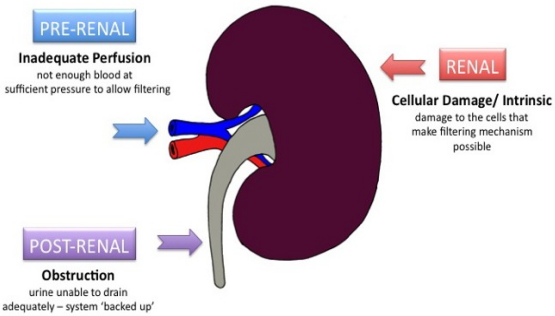


Figure 11: The pathogenesis of AKI (www.ole.bris.ac.uk)

Pre-renal AKI – This is also known as **volume –responsive AKI**, which is the common form of AKI. It is usually associated with reduction in GFR, with intact renal tubule which acts avidly to conserve salt and water in the face of reduced renal perfusion. The reduced urine output (oliguria) is a self-protective mechanism aimed at preserving the integrity of the renal tubules, and maintaining intravascular volume, a syndrome referred to as ***"acute renal success"***.[14]

They are caused by Gastroenteritis, Birth Asphyxia, Dehydration, Haemorrhage, Burns, Third space losses eg sepsis, trauma, Nephrotic syndrome or Cardiac failure.[18]

B. Intrinsic or Intrarenal AKI- This is characterized by structural damage to the renal parenchyma, most commonly from prolonged pre-renal AKI or severe glomerular disease. The causes include; *Glomerulonephritis- Post-Streptococcal acute Glomerulonephritis, Systemic Lupus Erythematosis, Henoch Schonlein Purpura, HIV, Hepatitis B &C. Acute Tubular Necrosis, Nephrotoxic drugs-Aminoglycosides, NSAID, ACE-Inhibitors, Severe Malaria – Blackwater fever and sepsis, Interstitial Nephritis-antibiotics, anticonvulsants, Thrombotic microangiopathy- Haemolytic Uraemic Syndrome, Cortical Necrosis- Renal Vein Thrombosis, Renal Artery Stenosis and Tumour lysis syndrome*

C: Post renal or Obstructive AKI –is characterized by acute obstruction of the urinary tract either as a congenital or acquired anatomic obstruction. The causes are; *Posterior Urethral Valves, Bilateral ureteral Obstruction- Pelviureteric junction obstruction (PUJO), Vesicoureteric junction obstruction (VUJO),Ureterocele , Urethral Stenosis, Calculi, Leukaemia and Mismatched Blood Transfusion.*

Incidence & Prevalence.

The lack of consensus on the definition of AKI has led to a variety of quoted incidence rates in the literature.[14,19-27] In developed countries it ranged from 2.7% (defined as need for dialysis) in Italy among children undergoing cardiopulmonary bypass surgery, to 3.2 per 100,000children in United Kingdom and 44.7 per 1000 admissions among children in Paediatric Intensive Care Unit (PICU) in Canada.[28] In Africa, the prevalence is variable and under reported. A prevalence rate of 1.2% was reported among paediatric admissions in Morocco.[20]

In 2003 we studied patients aged 5days to 16years (mean 5.6 ± 4.7 years) with AKI over an 18 year period (January 1985 to December 2003) seen in University of Port Harcourt Teaching Hospital (UPTH). There were 211 patients, 138 (65.4%) males and 73 (34.6%) females (M:F, 1.9:1). We reported a hospital prevalence of 11.7 cases of AKI /year.[29] Majority, 184 (87.2%) patients had reduced urine output, while 39 (18.5%) had hypertension. **The causes of ARF were age-related and mainly from preventable conditions.** Seventy-six (36.0%) were infants and 54(25.6%) were over 10years old. The neonates had ARF from severe birth asphyxia 27 (35.5%), septicaemia 17 (22.4%), with tetanus 4 (5.3%) and congenital malformations 11 (14.5%). As shown in Figure 12, gastroenteritis was the commonest cause of ARF. Sixty-one (28.9%) and 29 (13.7%) patients had ARF from gastroenteritis and malaria respectively. Eighty-five patients died in the hospital giving a high mortality rate of 40.5%.

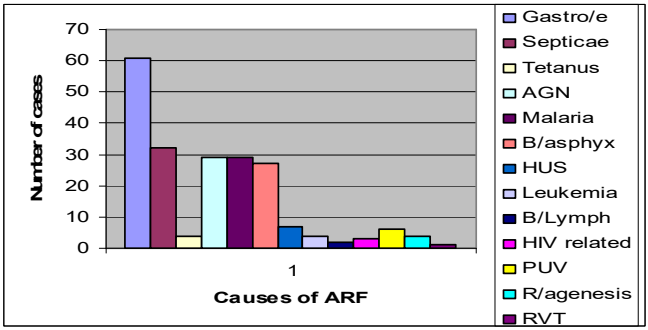


Figure 12: Causes of acute renal failure in children in UPTH

Key: AGN-Acute Glomerulonephritis, HUS-Haemolytic Uraemic syndrome, HIV-Human Immunodeficiency Virus, PUV-Posterior Urethral Valve, RVT-Renal vein thrombosis.

Rising incidence of AKI

We did a prospective study over a 4-year period of cases of AKI seen from 2008-2011. The study revealed an increase annual incidence from 15 to 20cases/year, with male preponderance as shown in Figure 13.This compares with a recent study in Abuja showing a progressive increase in the diagnoses of renal diseases during the study period, from 3.1% in 2013 to 5.4% in 2016. [30]

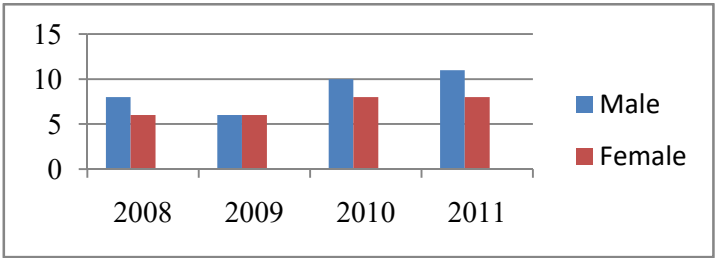


Figure 13: Incidence of AKI in children in UPTH (2008-2010)

Acute Glomerulonephritis (AGN)

Acute Glomerulonephritis is an important cause of intrinsic AKI. Earlier studies in the nineties showed yearly increases with seasonal variations in Africa.[21,31] The post infectious AGN is prevalent in Sub-Saharan Africa mostly due to *Group A- Beta haemolytic streptococcus* infection causing passage of coke coloured urine. We did a prospective study of all children admitted with AGN over a 2 year period from June 2006 to 2008.[32] A total of 31 patients aged 3 to 16 years were seen, with annual incidence of 15.5cases/year. Table 3 shows the age and sex distribution of these patients. AGN occurred with equal sex distribution, and more in those aged >5years.

Table 3: Age and sex distribution of patients with AGN in UPTH

Age(years)	Male(%)	Female(%)	Total(%)
<5	3(18.8)	5(33.3)	8(25.8)
5-10	8(50.0)	6(40.0)	14(45.2)
>10	5(31.2)	4(26.7)	9(29.0)
Total	16(100)	15(100)	31(100)

The highest cases occurred during the dry cold windy (Harmattan) season of October to February in 19(61.3%) patients. Twenty-four (77.4%) were from low socio-economic class. Sore throat was the commonest infection preceding AGN in 8(66.7%) while 2(16.7%) had skin infection, and 2 (16.7%) had both sore throat and skin infection. Complications are common in our environments such as AKI 12 (38.7%)and Nephrotic syndrome 4 (12.9%).[33] Twelve (38.7%) patients developed AKI, with a mean duration of admission of 12.3±9.6days (range from 5-46days). The outcome was good as 29(83.9%) patients survived and 3(9.7%) died in the hospital.

Drug- induced AKI

AKI may follow use or abuse of some prescribed drugs including gentamycin antibiotics, some antihypertensives like angiotensin converting enzyme inhibitors, or pain killers such as non-steroidal anti-inflammatory agents (NSAIDs) like Ibuprofen or non- prescribed agents like herbal concoctions, such as those containing aristolochic acids. [34] We recorded an epidemic of AKI in several Nigerian infants between September and December 2008 from diethylene glycol (DEG) contamination of "My pikin" (MP), a teething powder. DEG is an industrial solvent with a sweetish taste commonly used in

the commercial preparation of antifreeze, brake fluid and some dyes. It is a cheap solvent used by some pharmaceutical companies as a diluent in syrups. It is nephrotoxic and has caused many epidemics of AKI due to contamination of drugs in several countries including Nigeria in the ninetees,[35] the United States of America (USA), South Africa, India, Bangladesh, Haiti, and Panama.[36]

"My pikin"syrup contained paracetamol (120mg/5ml) and diphenhydramine (6.25mg/5ml) and was used to treat fever attributed to teething in young children. Six of these children aged 6 to 9months presented to UPTH, while the others presented to Ahmadu Bello University Teaching Hospital (ABUTH) Zaria and Aminu Kano University Teaching Hospital Kano, in the North West zone; Lagos University Teaching Hospital (LUTH), Lagos State University Teaching Hospital, Nigerian Army Reference Hospital Yaba, Lagos, and University College Hospital Ibadan (UCH) in the South West zone; University of Nigeria Teaching Hospital, Enugu in the South East zone and National Hospital Abuja, FCT.

We carried out a multicenter study to determine the impact of this drug-induced AKI over a 6-month period. Sixty (50.4%) of 119 children with AKI seen during the study period had ingested "My pikin" teething syrup. Many 25 (41.7%) children had been given MP because they were ill (mainly fever, diarrhea, and vomiting) and their parents assumed the illnesses were caused by teething. Fifteen other children (25%) who were not ill had been given MP to prevent teething problems. Mortality was very high overall with 57 (96.6%) of 59 died (within minutes to 13 days after admission) and one signed against medical advice. We did peritoneal dialysis on all the children that presented in our hospital, but none survived.[37]
The epidemic was given an urgent attention through the mass media including Vanguard newspaper publication (Figure 14).

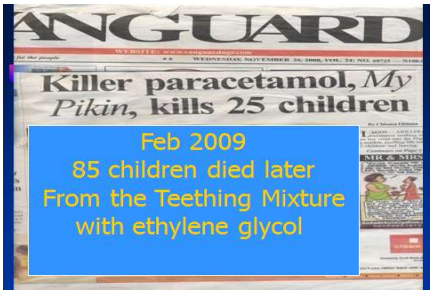


Figure14: Vanguard Newspaper advert on the Killer drug in 2008.

National Agency for Food and Drug Administration and Control (NAFDAC) was immediately alerted. This led to investigations, and public alert banning the sale of "MP" in Nigeria. The manufacturing facility was subsequently closed and the drugs withdrawn from retail outlets, clinics, and hospitals. We were able to control the mass casualties by our collective efforts and vigilance.

Bedwetting (Enuresis)

Bedwetting is a common cause of emotional problem in children, and may be a sequel of organic problems in 5 – 10% including poorly treated urinary tract infection.[38] It may result from excessive production of urine during the evening and night hours (nocturnal polyuria), reduced bladder capacity, or arousal dysfunction, sleep disorders, defective CNS regulatory centers, detrusor overactivity, or a defect intrinsic circadian control of bladder function. The cause of nocturnal polyuria are heterogeneous and involve reduced nocturnal plasma vasopressin levels and renal factors such as increased GFR and solute excretion (e.g. sodium) as well as increased prostaglandin PGE2 excretion.[38,39] Enuresis may be daytime (DE), nocturnal enuresis (NE) or combined, while the aetiology may be primary or secondary. Primary nocturnal enuresis (PNE) occurs when a child has never achieved a six

month period of continuous nighttime bladder control while secondary nocturnal enuresis (SNE) refers to a child who has experienced a minimum six month period of continence before the onset of bed-wetting.

We studied school children in Port Harcourt, and found 25.3% and 23.2% of children aged 10 - 19 years in secondary and primary schools respectively to have enuresis.[40,41] It was significantly higher in males than females (27.4% versus 19.0%, p =0.002). Majority 65 (52.4%) had secondary NS and 59 (47.6%) had primary NE. Eighty-eight (71%) had no organic cause to the enuresis, while poor family structure mainly parental separation (9.7%), divorce (12.9%) and death in the family (3.2%) occurred in SNE. We found enuresis more in those from polygamous homes, and it caused emotional problem in 60.5% of the students and their parents.[42] In 21.8% of the cases punitive measures of beating were applied as a form of deterrence.

The studies revealed that bedwetting decreased with age and majority had no organic causes. We discourage the use of punitive measures as it may reduce the self-esteem of the child.

Urinary tract infection (UTI)

The infection of the urinary tract is a common problem in children, and may involve the kidneys (acute pyelonephritis) or the lower urinary tract (cystitis, urethritis) .[43] Acute pyelonephritis (APN) may lead to irreversible renal scar in 50-65% of affected children especially if not properly treated resulting to chronic kidney disease. [44]

UTI may occur in children with normal urinary system or those with abnormal urinary system. During the 1st 3months of life, UTI is more prevalent in males (M: F ratio is 2.8–5.4: 1) and beyond infancy there is a striking female preponderance (M: F ratio of 1: 10).

The risk factors for UTI include;

- Female sex, anatomic abnormalities of the urinary tract causing urinary stasis (obstructive and unobstructive) eg posterior urethral valves, pelvi-ureteric junction obstruction(PUJO), vesico-ureteric junction obstruction (VUJO), Ureterocele, ureteral stricture. bladder diverticula, neurogenic disorders such as spina bifida, calculi, hydronephrosis, vesico- ureteric reflux (VUR)
- Chronic constipation, wearing tight pants or underwears, bubble baths, pinworm infestation, poor toilet habits, wiping from back to front in females
- Urethral catheterisation, indwelling catheters, male non-circumscision and sexual activity

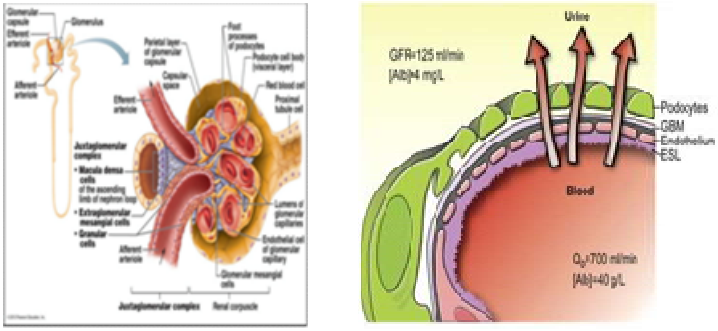
The diagnosis of UTI requires collection of mid stream urine into a sterile bottle, which must be sent to the laboratory within 1hour of collection, to ensure correct diagnosis with pathogenic bacterial isolate.

In 2001, we studied 66 children with a diagnosis of UTI over a four-month period to determine the commonest organism and the influence of Instruction about the method of urine collection and storage on the prevalence of UTI.[45] We found that the commonest cause of UTI was *Klebsiella*, and the method of urine collection was explained to 68.2% of the patients/ relatives. Despite the explanation, 14(21.2%) of the patients collected the urine sample wrongly and 48(72.7%) stored the urine sample longer than one hour before analysis. The reasons given for delayed submission of urine were distance from the hospital (70%), traffic congestion (20%) and lack of knowledge (10%). Significant bacteriuria was more prevalent in 72.7% of patients who submitted their urine sample late. We concluded that greater proportion of urine samples sent for analysis were not properly collected by the patients, and there was inadequate instruction by health

workers on the correct methods of urine collection and storage. We recommended that urine sample for culture should be collected in the hospital to avoid the delay in submission due to travel distance and traffic congestion common in Port Harcourt.

Nephrotic syndrome (NS)

Nephrotic Syndrome is the commonest chronic glomerular disease in children. It results from loss of negatively charged heparin sulfate proteoglycans in the glomerular basement membrane and the effacement of podocytes (Figure



15),leading to loss of large amount of protein especially albumin (>40mg/m^2/hour) in the urine .[46]

Figure 15: Glomerular basement membrane (www.memorangapp.com)

Congenital NS occurring before the age of 3months mainly due to genetic mutation of podocyte proteins or intra-uterine infections by syphilis, rubella, toxoplasmosis, cytomegalovirus and HIV, though rare has been reported in Nigerian infants, with challenges in management and poor outcome.[47-49] In 2015, we reported a case of infantile NS in an 8month old female in Port Harcourt.[50] Numerous studies have reported cases of childhood NS (> 1year) mostly sporadic with only a

few familial cases in the literature.[50-56] The patients present with varying degrees of body swelling (Figure 16).

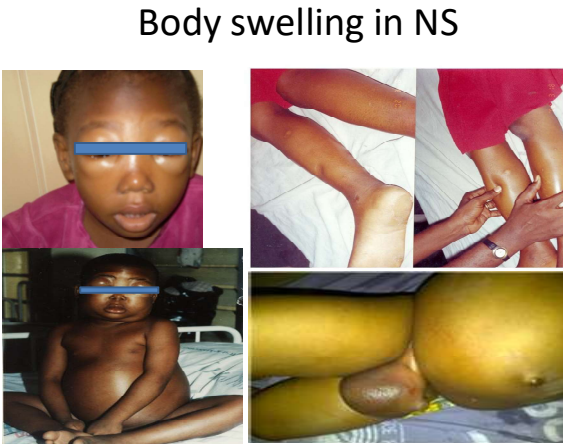


Figure 16: The clinical presentation of childhood NS (varying degrees of oedema)

Fanconi et al[57]reported the first case of Familial Nephrotic syndrome (FNS) in 1951 in six families with 13 affected siblings in China. Genetic mutation of the podocyte protein as well as *APOL* 1 gene have been implicated in the familial NS (FNS), the latter being of African descent.[58]

We presented the first case of familial NS involving 2 children (4-year old male and 11-year old female) in a non-consanguineous family of 5 children from Owerri, South-Eastern Nigeria at an International Paediatric Nephrology Association (IPNA) Scientific Congress at New Hilton Hotel, New York, USA on the 20thSeptember, 2010. The presentation stimulated a lot of discussion and public interest leading to an offer by Prof Rasheed Gbadagesin, a Paediatric Nephrologist in Durham, USA who sponsored the genetic testing of the entire family for mutational studies. The study was published in a reputable journal and has been cited as the first time mutational analysis of NPHS2, WT1 and *APOL*1 in Nigeria,

putting us in the world map of genetics in Paediatric Nephrology.[59]

The pattern of presentation, histopathology and response of childhood NS to steroid varies widely.[51,57-60] It may be steroid sensitive or steroid resistant NS. An earlier study in western Nigeria showed rarity of minimal change disease with none response to steroid. However, Eke *et al* [52] at the same time reported favorable response of NS to prednisolone in Southern Nigeria. We have continued to observe steroid sensitive NS in Port Harcourt decades after the earlier report. We studied 28patients with NS from 1999-2004, 20 had idiopathic (INS), of which 16 (57.1%) were steroid sensitive (SSNS).[61] This study has encouraged the use of steroid as first line drug in the management of NS even in the tropics, and stimulated similar studies in other centers. The steroid resistant NS (SRNS) are mainly FSGS, and mostly progress to end stage renal disease.[62,63]

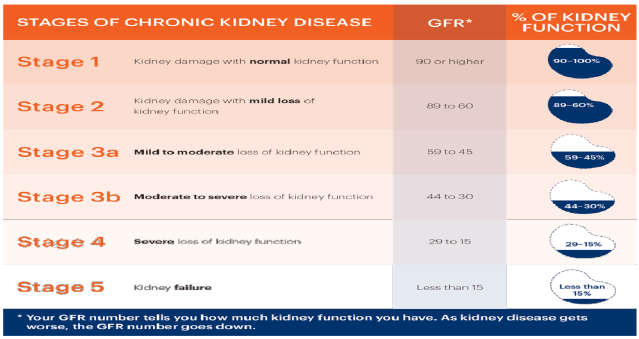
CHRONIC KIDNEY DISEASE (CKD)

CKD is one diagnosis we dread as Nephrologists working in resource-poor countries with limited facilities for renal replacement therapy. Almost all patients with ESRD die within few years of diagnosis, and thus CKD is regarded as a **"death sentence".** Mr Vice-Chancellor Sir, the diagnosis of CKD reminds us of this statement in Job 3 : 25; (KJV) ***"For the thing which I greatly feared is come upon me, and that which I was afraid of is come unto me".***

CKD is a progressive, persistent and irreversible kidney failure due to structural abnormality of the kidney lasting more than 3months. Historically, chronic renal insufficiency was used to describe glomerular filtration rate (GFR)<60ml/min/1.73m^2).[64] Since 2001, the National Kidney Foundation Kidney Disease Outcome Quality Initiative (NKF-K/DOQI) provided CKD classification in staging renal dysfunction in children > 2years

of age into five stages based on the degree of kidney impairment (Table 4). This classification system is based on the level of kidney function as estimated by glomerular filtration rate (GFR) regardless of the underlying pathology.

Table 4: Stages of chronic kidney disease (www.kidney.org/atoz/content/gfr)



CKD is a spectrum of kidney disease ranging from renal damage with a normal GFR (stage 1) to end stage renal disease (stage 5) necessitating renal replacement therapy. At GFR of 60ml/min/1.73m^2, a critical set-point is reached beyond which progressive renal functional decline is inevitable even after primary disease process has become quiescent.

Pathophysiology and Pathogenesis.

Regardless of the etiology, CKD is characterized by renal fibrosis-glomerulosclerosis and tubulointerstitial fibrosis with progressive decline in glomerular filtration rate (GFR), reduced urine output and the systemic complications (Figure 17). [65]

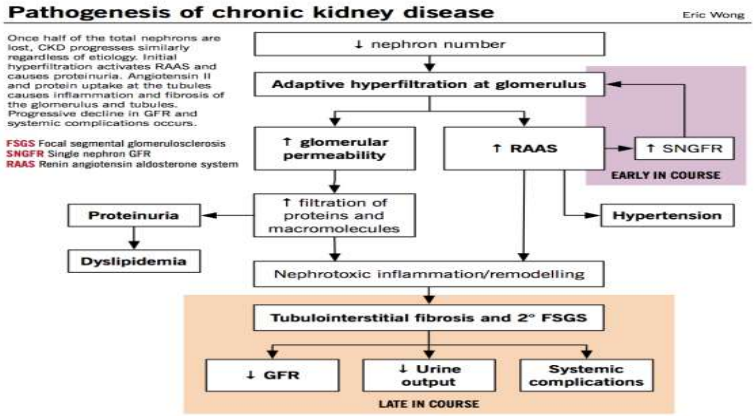


Figure 17: Pathogenesis of CKD (www.pathophys.org/ckd)

Epidemiology

The incidence and prevalence of CKD is on the increase globally in both children and adult population. In most developing countries including Sub-Saharan Africa (SSA) the burden is underreported, because majority of early stages are asymptomatic and do not present to the hospital. [66] Furthermore, lack of data on pediatric kidney diseases and absence of renal registries in general affect accurate epidemiological data. Majority of the studies on CKD are hospital-based and they form a tip of the iceberg, which do not represent the burden of the disease.[19,21-28,66] In Port Harcourt, Nigeria, Eke and Eke[21] noted that 2.5per million children per year were expected to develop CKD.

We did a 15 -year review of 45 children below 16years of age who presented with CKD to UPTH from 1985-2000. They aged 6months to 16 years with a mean age of 9.1 years. The prevalence rate of CKD increased from 12.5 during the 1985-1995 to 15 per million children per year after 1995.[67] We found Glomerulopathies in 23 (53.3%) mainly Chronic glomerulonephritis 13(28.9%) and steroid resistant Nephrotic

syndrome 8(17.8%) as the common causes of CKD in older children≥ 10years, while congenital disorder mainly PUV(28.9%) in those <5years of age (Table 5). Our finding compares with report from Turkey and other countries in the Middle East where CAKUT was the leading cause of CKD (47–62%) mainly the uropathies.[66] The high proportions of glomerulonephritis may be related to high prevalence of bacterial, viral, and parasitic infections that commonly affect the kidneys in developing countries.

Table 5: Causes of Chronic Renal Failure in UPTH (1985-2000).

Primary renal disease	No. of patients(%)	Males-28	Females - 17
Congenital disorders (Posterior urethral valve)	13(28.9)	13	-
Acquired disorders Glomerulopathies Vascular nephropathies (HUS, SCD, Malignant HTN)	 23(53.3) 7(15.6)	 9 4	 14 3
Non-obstructive PN	1(2.2)	1	-
Bladder rhabdomyosarcoma	1(2.2)	1	-

Posterior urethral valve (PUV) was the commonest cause of obstructive uropathy (80%) seen in UPTH between October 1997 and 2002, and bladder rhabdomyosarcoma accounted for 20%.[68,69] PUV is a congenital abnormality of the male prostatic urethra with persistent valve that partially or completely impedes urine outflow, with consequent bladder hypertrophy, hydroureters and hydronephrosis (Figure 18).

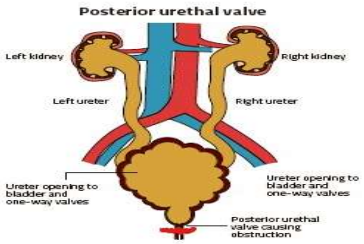


Figure 18: Posterior urethral valve (www.pressreader.com)

The incidence is 1 in every 4000-5000 live male birth in developed world, and it accounts for 20% of childhood ESRD.[70] It presents *in utero* with maternal oligohydramnious due to reduced foetal urine production with resultant respiratory and limb abnormalities as shown in Figure 19.

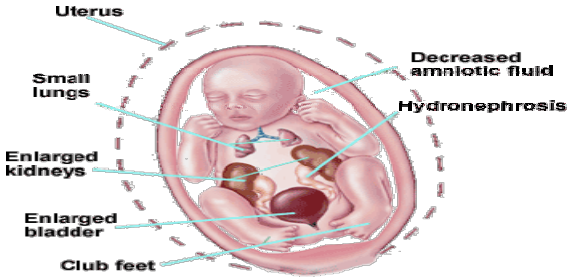


Figure 19: Features of PUV in a foetus (www.fetalhealthfoudation.org).

The diagnosis is made by routine prenatal screening ultrasound done in the second and third trimester. We did a 2 year review of children ≤16years with PUV from January 2007 to December 2009 in the department. PUV contributed to 15(0.04%) out of 36,700 paediatric patients seen during the study period, giving an incidence of 1:2447 patient population.[71] The PUV patients were aged 3days to 15 years (mean of 22.8±19.4months). Symptoms started in the first week of life in 11 (73.3%) patients, but there was delayed

presentation to the hospital. Only 4 (36.4%) patients came during the neonatal period, 12 (80%) in infancy and 3(20%) after one year of life. Only one case (6.7%) was diagnosed in-utero. The commonest symptom was poor urinary stream with dribbling of urine in all patients (Figure 20). The urine stream contrasts with the flow seen in the "Mannequin pis".

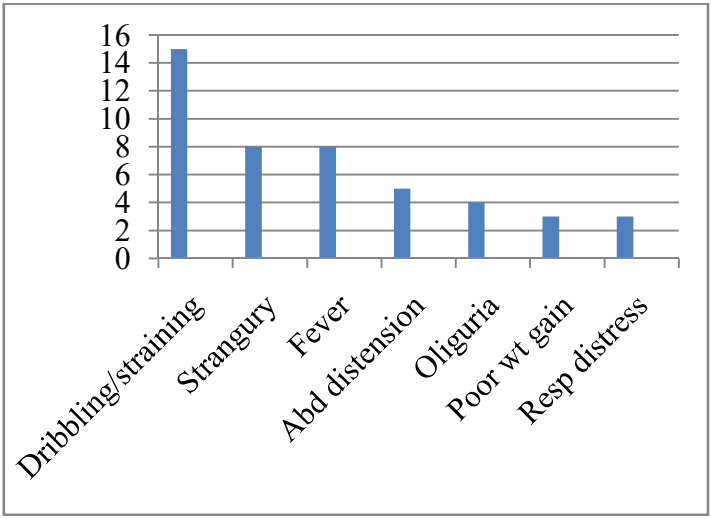


Figure 20: Symptoms of patients with PUV

Urinary tract infection [10 (66.7%)], acute renal failure [7 (46.7%)] and end stage renal disease [2 (13.3%)] were the complications. Among the 2 patients with ESRD, only one patient could afford renal transplantation which was done in India and he comes to UPTH for post transplant care whenever in the country. Three (20.0%) patients died while 5 (33.3%) were lost to follow up.

Our findings confirmed that prenatal diagnosis of PUV was very low (<10%) in our environment with delayed diagnosis and late presentation to the hospital.

Human Immunodeficiency Virus Associated Nephropathy (HIVAN)

HIVAN is a chronic renal manifestation of HIV infection, an important cause of CKD and ESRD in our children. With increasing survival of HIV-infected children, there has been a rising prevalence of HIVAN, with predominance route being mother to child transmission (MTCT).[72] Although the infection is acquired early in life, the patients tend to grow well and reach the ages of 2-10years before they develop renal symptoms. After which they deteriorate rapidly into ESRD and death ensues.

In 2008, we reported the first study of HIVAN among Nigerian children and one of such studies in Africa.[73] They were ten patients aged 5months to 15years (mean 6.8± 6.2years), with a peak age of 5-9years seen from January 2000 to October 2006. The diagnosis of HIVAN was based on the presence of persistent proteinuria of >1+ with one or more of the following; abnormal microscopic examination of the urinary sediments showing proteinuria, presence of enlarged echogenic kidneys on ultrasound and histologic finding of collapsing focal segmental glomerulosclerosis on renal biopsy. Nine (90%) of the patients were in renal failure, while 7(70%) died. Renal disease was the first manifestation of HIV infection in six (60%) patients, whereas diagnosis was confirmed at autopsy in 3 patients.

The research highlighted the importance of routine urine check of all children with HIV infection for early detection and prevention of CKD. Based on the report, we did routine urinary screening for early marker of CKD in 50 HIV patients in UPTH, and found microalbuminuria in 6 (12%) of these patients, supporting being proactive in early detection of CKD among HIVpatients.[74]

Our study on HIVAN was published in a reputable journal and has been cited by many authors. It has contributed to knowledge in the field of HIV infection, leading to my invitation to join the Editorial Board Member of Journal of Paediatric Diseases, excerpts:

"Dear Ifeoma Anochie, I represent the Editorial Office of EnPress Publisher LLC., an independent and international publication house from the United States.

Recently, our publishing team came across your article; "Human immunodeficiency virus-associated nephropathy (HIVAN) in Nigerian children" published in Pediatric Nephrology and found your publications highly impactful. Therefore, we are delighted to invite you to join the distinguished Editorial Board Member of our journal, Journal of Pediatric Diseases. We believe that your research will greatly contribute to not only the knowledge of your expertise but also the establishment of our journal." (Jim Williams, Editorial Office, Journal of Pediatric Diseases 2019).

Risk factors for CKD

These include modifiable and non-modifiable factors.

Non-Modifiable factors

1. *Preterm*- Babies delivered before 36weeks gestations are at risk of CKD due to reduced nephron number as nephrogenesis is completed by 36week of gestation. Thus premature delivery affects nephron number and function with increased incidence of hypertension, hyperlipidaemia and CKD in adult life.
2. *Low birth weight (LBW*)- LBW even after correction for gestational age is associated with increased risk of CKD due to low nephron number. The proposed mechanism linking low nephron number and CKD is consequent upon

intraglomerular hypertension leading to glomerulosclerosis.

3. *Ethnicity*- Racial differences may be attributed to genetic, environmental and/or socioeconomic factors. African Americans experience a disproportionately greater burden of ESKD than Caucasians and other minority groups.[65] This is attributed to higher incidence of hypertension-attributed ESKD (HA-ESKD), focal segmental glomerulosclerosis (FSGS) and HIV-associated nephropathy (HIVAN) in African American. Lupus Nephritis and HIV nephropathy are also more aggressive in this group
4. *Age*- Age per se is not an independent risk factor in paediatric population, although it is commonly perceived that renal function deteriorates more rapidly around the time of puberty especially in those with renal hypodysplasia.
5. *Sex*-Obstructive uropathies are more prevalent in males while urinary tract infections are more in adolescent females.
6. *Familial-(Hereditary or Genetic)*- Genetic mutations of the podocyte proteins, and abnormalities of APOL 1 and MHY49 located on chromosome 22 may predispose individuals to CKD. APOL1 is a member of a family of apolipoproteins which consists of 6 other proteins that provide innate immunity by protecting against Trypanosoma brucei infection. Two coding sequence variants in APOL1 have been shown to associate with kidney disease in a recessive fashion common in Yoruba descent of Nigeria.[59]

Modifiable Factors

1. *Obesity*-Precursors to CKD may also be components of metabolic syndrome. Morbid obesity is associated with a significant glomerulomegaly and glomerulosclerosis even in the absence of overt diabetes. Rural-urban migration, sedentary lifestyle, poor diet laden with high carbohydrate and fat are associated with obesity in children.
2. *Proteinuria*- has been identified as independent determinants of renal function decline and CKD progression. It may be a marker of glomerular damage, and it is the commonest urinary abnormalities seen in CKD.
3. *Hypertension*- is a common manifestation of many paediatric chronic kidney diseases .[75]
4. *Anaemia*- This is an important risk factor for the progression of CKD, due to hypoxia and oxidant stress contributing to renal fibrosis.
5. *Dyslipidaemia*- hyperlipidaemia is a predictor of renal deterioration.
6. *Hyperuricaemia*- Elevated uric acid level may be seen in CKD. In addition to urate nephropathy due to intratubular deposition, uric acid may damage the smooth muscle and vascular endothelial cells leading to renal dysfunction.[68]

HOW WE CARE FOR KIDNEY DISEASES.

Mr. Vice Chancellor Sir, the burden of kidney disease is enormous, and the care is quiet challenging especially in Sub-Saharan Africa and Nigeria in particular. My mentor, Prof Felicia Eke at the 54th Inaugural series in 2006 expressed these challenges as the agony of Paediatric Nephrology.[76]

Quote **"Each of us knows that we have an obligation to care for the old, young and the sick, we stand stronger when we stand with the weakest among us"** by Sarah Palin. The goal

of our care is to make a defendable diagnosis and provide prompt treatment in order to restore normal renal function, and good quality and quantity of urine.

History and physical examination

In the history, we explore the symptoms with emphasis on the volume of urine, including the number of wet pampers in infants, the colour of urine, smell, if foamy and the urinary stream (in males) among other presenting complaints. Antenatal and delivery history is important to search for risk factors such as prematurity, low birth weight and birth asphyxia.

"In questioning each patient, I always brought the conversation back to urine, no matter the primary problem. Whether the issue was vomiting, diarrhea or cough, I invariably asked how much the patient had urinated lately" Dr Jonathan Reisman 2016.

The clinical presentations of children with kidney diseases are variable depending on the aetiology, duration of illness, interventions given and co-morbidities. **Patients with CKD stage 1-2 are mainly asymptomatic**, with or without biochemical abnormalities. From CKD stage 3, a majority would develop biochemical abnormalities, signs such as body swelling, chronic hypertension, stunted growth, moderate to severe anaemia and renal rickets (osteodystrophy) (Figure 21).

Figure 21: Genu valgum (Knock knee) from renal osteodystrophy in a 15year old with PUV

Investigations.

Urine examination stands out as a very valuable tool and first step in the diagnosis of kidney disease. We search for every drop of urine to carry out **bedside urinalysis**, which involves a macroscopic examination of urine for the appearance, dipstick examination, microscopic and chemical analysis.

Dipstick Urinalysis (UA)- is convenient, easy to perform and interpret, and cost-effective for determination of pathological abnormalities in the urine. It provides a lot of information about the kidneys and the urinary tract or other systemic diseases, thus referred to as **"a poor man's kidney biopsy"**. It is done with a Combi test strips which is dipped in the urine to check for colour changes in each square of the dipstick, especially for presence of protein, blood, leucocytes and nitrite (Figure 22).

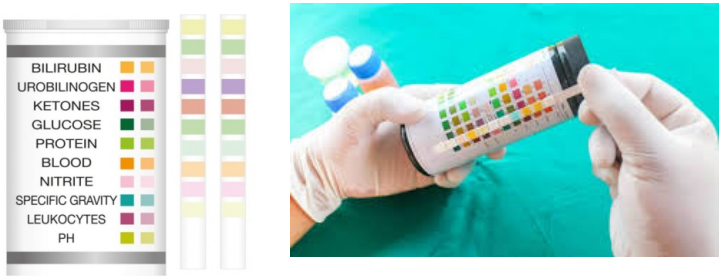


Figure 22: Combi -10 test strip and dipstick urinalysis

Combi-10 comprises chemical pads/reagents that test for ten different parameters in the urine.

The UA strips provide qualitative results as either positive or negative, while some are semi-quantitative indicating the estimate of the concentration of the substance in the urine as; trace, 1+, 2+, 3+ and 4+ (Table 6).[77,78] Early morning urine sample is preferred to exclude orthostatic proteinuria.

Table 6-The semi-quantitative dipstick test for protein on urinalysis

Proteinuria	**Concentration**
Negative	0 to <15mg/dl
Trace	15 to <30mg/dl
1+	30 to <100mg/dl,
2+	100 to <300mg/dl
3+	300 to <1000mg/dl,
4+	≥1000mg/dl

Dipstick UA has some limitations based on the possibility of false positives and false negatives results (Table 7). One important limitation is that it primarily detects albumin, and not low molecular proteins.[78]

Table 7- Causes of false positives and false negatives results on Urinalysis

Urine dipstick test	False positives	False negatives
Urobilinogen	Alkaline urine	Broad spectrum antibiotics, prolonged standing in light, discoloured urine
Bilirubin	Rifampicin	Ascorbic acid, prolonged standing in light
Nitrite	Urine contamination, drugs that turn urine to red or orange, gross haematuria.	Inadequate dietary intake of nitrate (vegetables), non nitrate producing organism (enterococci, staphylococci, adenovirus etc), frequent voiding , reduce incubation time in the bladder, ascorbic acid and high urobilinogen.
Blood	Oxidizing contaminants eg hypochlorites.	High ascorbic acid, large nitrites, high SG.
Protein	Alkaline urine, concentrated urine, presence of cells/bacteria in the urine	Dilute urine, low MW protein, mainly globulins or Bence Jones protein. (non-albumin)
Specific gravity	Contaminants	None
pH	High-from urease producing organisms eg *Proteus Mirabilis,* prolonged standing of urine.	Low-from mixing of reagents from adjacent test pads.
Glucose	Oxidizing agents in the urine container	Ascorbic acid, high SG,exposure to humid environment
Ketones	Drugs like captopril	Prolonged standing of urine, moisture on test pads
Leukocyte esterase	Contamination with vaginal fluid, oxidizing agents.	Ascorbic acid, high protein, high glucose, high SG, drugs – cephalosporins

In 2010 we did a cross-sectional study to evaluate the use of dipstick urinalysis test for leukocyte esterase (LE) and nitrite as a screening tool in the diagnosis of UTI among children aged 2 to 15years in UPTH. Out of 139 children studied, the LE dipstick correctly identified 17/33 children with UTI, with 51.5% sensitivity and 79.2% specificity. The nitrite dipstick

test had 73% sensitivity and 75.5% specificity. The combination of LE and nitrite correctly identified 24/33, with 73% sensitivity and 75.5% specificity.[79]

The study confirmed a high sensitivity of dipstick urinalysis in diagnosing UTI in the presence of combined LE and nitrite. This is relevant in settings where laboratory services are unavailable for urine microscopy and culture to confirm UTI, thus enabling prompt treatment with empiric antibiotics to prevent chronic pyelonephritis and ESRD.

Microscopic urinalysis helps to detect the presence of cells and cellular debris, casts, bacteria, and crystals in the urine sediment examined under a light microscope. The casts can be missed if microscopy is not performed within 30 minutes after voiding, thus fresh voided urine is required for microscopy. The presence of blood (haematuria) on dipstick is usually confirmed by urine microscopy.

Quantitative Urine Protein

Timed urine collection is required for quantitative analysis of proteinuria. The 24hours-urine collection has been considered a gold standard for quantifying urine protein excretion, but it is usually cumbersome and inaccurate. This is therefore replaced by a random spot urine protein/creatinine ratio (P/Cr) estimation which is more accurate than urinalysis, excluding the risks of false positives and negatives (Table 8).

Table 8- Quantitative Urine Protein measurement

Test	Normal	Abnormal	Nephrotic
24hour urine protein	<4mg/m^2/hr	4-<40mg/m^2/hr	≥40mg/m^2/hr or >50mg/kg/24hr
Urine P/Cr ratio (mg/mg)	≤0.2 (>2yr old) <0.5(6-24 months)	0.2- ≤ 2.0	>2.0
Urine Albumin/Cr ratio (mg/mg)	≤0.03		

Urinary indices –These measurements are used to differentiate the types of AKI as pre renal AKI or intrinsic kidney injury, mainly acute tubular necrosis (ATN) to guide treatment modalities (Table 9).

Table 9: Urinary Indices in AKI

Test	Pre renal	Intrinsic (ATN)
Urine osmolality(mOsm/kg)	>500	<350
Urine specific gravity	>1.020	≤1.020
Urine Sodium (mEq/L)	<20	>40
Fractional excretion of sodium(FeNa)	<1%(neonates) <2%	>1%(neonates) >2%
FeUrea	<35%	>35%
Urine/plasma Creatinine	>40	<20

Radiologic studies.

We do radiologic studies such as kidney and bladder ultrasound (KBUS), Micturating cystourethrogram (MCUG), cystoscopy, Computed Tomography scan (CT), Magnetic resonance Imaging (MRI), Nuclear studies such as (Mercaptoacetyltriglycine (Tc-99 MAG3) and Dimercaptosuccinic acid (Tc-99 DMSA) scan, and Urodynamic studies etc. In PUV, the KBUS shows thick walled, trabeculated bladder with elongated and dilated posterior urethra ("Key hole sign"). The diameter of the proximal urethra of more than 6mm is considered abnormal and highly sensitive (100%) and specific (89%) to the diagnosis of PUV.[80] MCUG is an important diagnostic tool for PUV, voiding dysfunction and VUR (Figure 23).

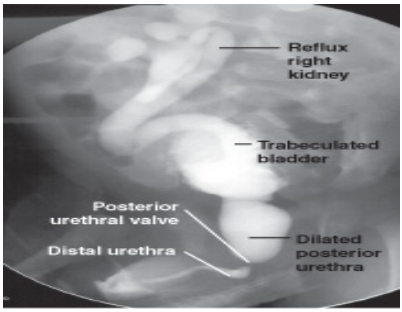


Figure 23: Micturating cystourethrogram of PUV (www. Pediatriccare.solutions.aap.org)

Laboratory studies- These include full blood count , serum electrolytes, urea and creatinine (old Jaffe method or enzymatic method), serum Cystatin C, serum calcium, phosphate, total protein, albumin, calcium, uric acid, serology (HIV, HBsAg, HCV), complements studies, antibody tests depending on the diagnosis. The common biochemical abnormalities are shown in Table 10.

Table 10- Biochemical abnormalities

Biochemistry test	**Findings**
Serum Electrolytes, calcium, phosphate, alkaline phosphatase (ALP)	High potassium level (hyperkalaemia), low sodium (hyponatraemia), normal or low calcium level (hypocalcaemia), high phosphate (hyperphosphataemia), low bicarbonate (metabolic acidosis), ↑ALP.
Urea and Creatinine Serum BUN/Cr ratio(mg/mg)	Elevated urea &creatinine >20=prerenal, 10-15=ATN.
Total protein/ albumin/ cholesterol	Low total protein and albumin levels, dyslipidaemia
Uric acid	High uric acid level
Parathyroid hormone (PTH)	Elevated PTH(Hyperparathyroidism)

Estimated Glomerular filtration rate (eGFR)

We estimate the GFR of patients to determine the level of kidney function, and extent of kidney disease using Schwartz and modified Schwartz formula: eGFR = k ht/ SCr in

ml/min/1.73m^2, where ht is height (cm),SCr is serum creatinine(mg/dl) and a constant k.[81,82] The other methods of estimating GFR such as the Modification of Diet in Renal Disease (MDRD) and Cockcroft-Gault formulas are inaccurate in children but preferred in adults. The eGFR is lower in newborns and increased with age until 2years where it stabilizes to adult range of 90-120ml/min/1.73m^2.[82]

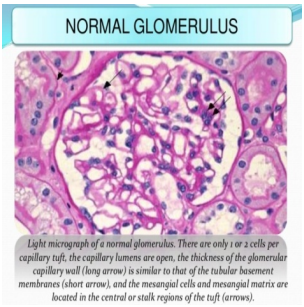
Kidney biopsy (KB)

Kidney biopsy is a very important procedure to determine the aetio-pathogenesis of kidney disease, guide further treatment and the prognosis.[83]The kidney tissues (native or transplant) are obtained by either an Open surgery or percutaneous (most common) route. We commonly perform percutaneous native KB in UPTH under local anaesthesia and light sedation of the patients, with direct ultrasound guidance. (Figure 24).

Figure 24- Kidney biopsy under Ultra Sound guidance

The procedure is invasive and therefore not a routine investigation except when indicated such as in; *Recurrent/persistent haematuria, proteinuria, Atypical NS, SRNS, AGN (Atypical of PSGN etc),AKI with Nephritis ,systemic diseases (SLE,HSP),vasculitis, Rapidly progressive GN, CKD of unknown cause, Follow-up of Disease & treatment with calcineurin inhibitors (CIN), Disease recurrence or rejection in transplanted kidney.*

Steroid resistant NS is the commonest indication for KB in our hospital**.** The kidney tissues obtained are examined under Light microscopy (LM), Immunofluorescence microscopy (IM) and Electron microscopy (EM) but unfortunately, we can only perform LM in UPTH. We did a KB on the 10/12 (83.3%) patients with SRNS among the 89patients with idiopathic NS from June 2006 –Dec 2012. [62] Focal Segmental Glomerulosclerosis (FSGS) (80.0%) was the commonest histology followed by Membranous GN (10%) and Membranoproliferative GN (10%) (Figure 25).



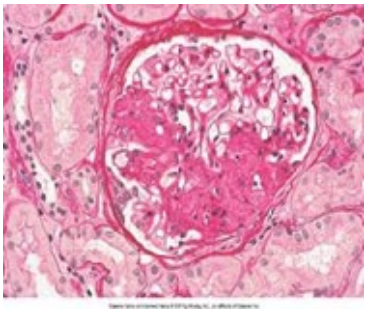


Figure 25 – Normal tissue FSGS

Genetic studies

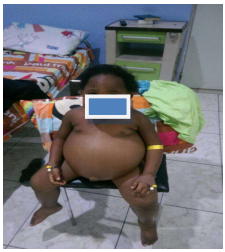
The use of genetic study has improved understanding of many kidney diseases especially SRNS and some rare diseases.[84] It may involve entire genome sequencing which represents the most comprehensive option, sequencing of its ~2 % coding part (whole-exome sequencing [WES]) or single gene analysis. The comprehensive gene analysis is more difficult, time consuming, and expensive than specific gene analysis, but has the advantage of being able to locate new, as yet undiscovered, genes. Mutations in NPHS2, WT1 and NPHS1 are the most common genetic causes of SRNS in Caucasians. Unfortunately, genetic studies are not done in Nigeria so we rely on laboratories outside the country.

Treatment

The treatment include medical and/or surgical approaches depending on the diagnosis, as well as renal replacement therapy.[16,64,85]

As part of medical treatment, conservative measures such as management of fluid and electrolytes, antibiotics for infections (UTI, pneumonia, peritonitis, and sepsis), antihypertensives to control blood pressure, 20% albumin infusion for NS with intractable oedema, corticosteroids and other immunosuppressives for SRNS are provided. Figure 26 shows the benefit of albumin infusion in Nephrotic syndrome. Patients with AKI and early stages of CKD are managed conservatively until renal replacement therapy is indicated.

Non-pharmacological measures are useful in those with bedwetting while pharmacological therapies are reserved for those with compromised self-esteem, and voiding dysfunction. The drugs include desmopressin acetate, anticholinergic drugs such as Oxybutinin chloride for overactive bladder, dysfunctional voiding or neurogenic bladder to reduce uninhibited detrusor contractions and hence enlarge functional bladder capacity (refer to Micturition reflex). Pharmacological treatment of enuresis is not recommended for children younger than 7years of age.



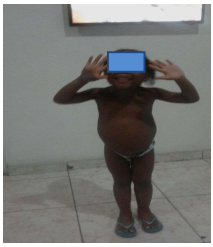


Figure 26: Before After Albumin infusion

We refer patients with CAKUT such as PUV to the paediatric surgeons and urologists for valve resection/ablation, and other surgical procedures. Some children with congenital NS may require surgical removal of a kidney (unilateral or bilateral nephrectomy) due to massive proteinuria. All patients with kidney diseases including those that had surgery must be followed up by the Nephrologists for life to aid early detection of CKD, and institution of measures to retard progression to ESRD.

Those with CKD are given some drugs to slow the progression of kidney damage to end stage renal disease.[85] These drugs are used to alter the modifiable risk factors like hypertension (ACE I , calcium channel blockers, diuretics), proteinuria (ACEi), anaemia(erythropoietin), hyperlipidaemia (Statin), and to control mineral bone disorder (CKD-MBD) as shown in Figure 27.

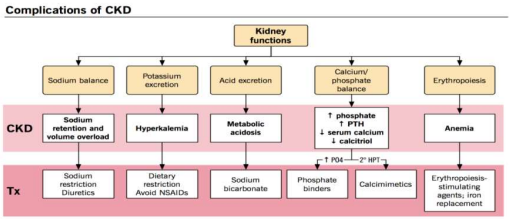
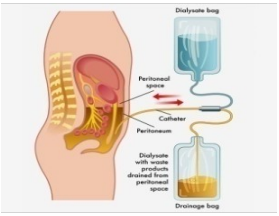


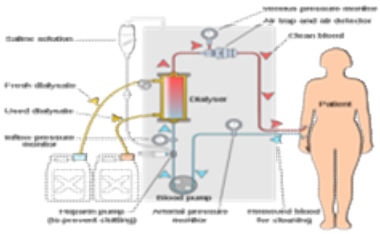
Figure 27- Treatment of complications of CKD (www.pinterest.com).

Renal Replacement Therapy (RRT).
Patients with AKI who fail to produce normal urine output following conservative management or those with ESRD are offered renal replacement therapy.[85,86] It includes Dialysis, Continuous renal replacement therapy (CRRT) and Kidney transplantation (KT).

Dialysis -This is the process of removing excess water, solutes, and nitrogenous waste substances (toxin) from the blood of patient whose kidneys can no longer perform their functions normally. It works on the principles of diffusion of solutes (solute clearance) and ultrafiltration of fluid across a semi-permeable membrane.
There are two main types of dialysis, peritoneal dialysis (PD) and haemodialysis (HD).The peritoneal membrane acts as the semi-permeable membrane in PD and the dialyzer (artificial membrane) in HD (Figure 28). During the process the accumulated nitrogenous waste substances such as urea, creatinine, potassium etc are removed from the body into the dialysate, while useful substances such as bicarbonate in the dialysate move into the patient's blood to correct metabolic acidosis.



(a) Peritoneal dialysis (PD)



(b) Haemodialysis (HD)

Figure 28- a & b

RRT in AKI

In AKI, the modalities of RRT include acute PD, intermittent HD (IHD) and Continuous renal replacement therapy (CRRT).[86,87] The CRRT include continuous arteriovenous hemofiltration (CAVH), continuous venovenous hemofiltration (CVVH), continuous venovenous hemodialysis (CVVHD) and continuous venovenous hemodiafiltration (CVVHDF), slow continuous ultrafiltration (SCUF) and slow efficiency dialysis(SLED), which are not available in our facility.

The choice of appropriate modality depends on the clinical status of the patients such as age, size, co-morbidities, urine output & extent of multiorgan involvement, resources /facility availability and individual physician beliefs.

Acute Peritoneal Dialysis was the modality first used for the treatment of patients with AKI because of its inherent advantages.[87] It is valuable in neonates, small infants and children less than 20kg, with no need for vascular access. It is done continuously in the hospital either manually or automated with a "Home choice" cycler machine. The number of exchanges required in PD may range from 6-24cycles in a 24-hour period, and continued until renal functions are restored, with increase urine output.

Intermittent HD and CRRT require vascular access (central venous access eg jugular, subclavian, femoral, brachial vein), dialysate composition, blood lines and dialyzers which vary depending on the patient's size and surface area. IHD provides rapid ultrafiltration and solute clearance, thus it remains an optimal form of dialysis in patients with severe fluid overload and severe hyperkalaemia. Intermittent haemodialysis is done in the Haemodialysis unit over 3-4hours /session daily until renal function is restored. However, HD is not feasible in infants and very young children <20kg in developing countries because of poor vascular access due to unavailability of small

catheters, dialysers and blood lines required to achieve adequate blood flow in these young children.[88]

CRRT is used for haemodynamically unstable children, and in those with multi organ system dysfunction due to gradual nature of fluid removal, and solute clearance which is by convection.

We perform acute dialysis in children with AKI in our hospital, especially PD in those less than 5 years and HD in the older patients (Figure 29).

Figure 29-APD in children with AKI including during "my pikin" poisoning.

RRT in CKD

This involves chronic dialysis and kidney transplantation (KT). Chronic Dialysis is generally started when the kidneys are working at less than 10% of their normal function. It is regarded as a temporary measure while waiting for KT. According to Kidney Disease Outcome Quality Initiative (KDOQI) guidelines, dialysis initiation should be considered at eGFR <15ml/min/1.73m^2 and strongly when eGFR <8ml/min/1.73m^2.[89]

Chronic PD is either as continuous ambulatory peritoneal dialysis (CAPD) or as any of several forms of automated peritoneal dialysis (APD) with a cycler namely continuous cyclic peritoneal dialysis (CCPD), intermittent peritoneal dialysis (IPD) and nocturnal intermittent peritoneal dialysis (NIPD).[89,90] Chronic PD is done daily at home and it is the

preferred dialysis in children with CKD in developed countries. The use of CAPD has been reported scarcely in poor-resource African countries, with first case in Senegal, Dakar.[90]

Chronic or Maintenance HD (CHD) is mostly done in the hospital, ideally three times in a week with a minimum of 10-12hours dialysis exposure per week for efficient regulation of fluid and electrolytes balance. The preferred vascular access is native arteriovenous fistula (AVF), but arteriovenous graft (AVG) and central venous access may be used.

Kidney or Renal transplantation is the standard/**permanent** treatment for patients with ESRD. It is a surgical procedure where a healthy kidney is transferred from a compatible donor to a recipient with ESRD (Figure 30). KT is a complex surgery, involving transplant surgeons, urologists, paediatric nephrologists, anesthetists, procurement teams and organ allocation personnel etc.

Types of KT

This depends on the type of donor of the kidney used in the transplant. It may be a **living donor** (related or non related) or **deceased donor** (formerly known as cadaveric).[91,92] Deceased KT may be from deceased brain dead (DBD) or deceased cardiac death donor (DCD).

Living related donor is the most common source of living donor kidneys in children, mainly from first degree relatives such as parents or adult sibling. The use of living unrelated (altruistic) donor is increasingly common in most developed countries and accounts for about 10% of all UK transplants. However, long term graft outcome of living related donor kidneys is superior to all other donor kidneys. Approximately 80% of KT patients worldwide live in Europe, Japan or North America, where all children with ESRD have access to RRT.[66]

Selection of donors requires blood group compatibility (ABO), tissue matching and careful assessment of the donor's cardiovascular and kidney health. Urological assessment and urodynamic studies are mandatory before KT for recipients with obstructive uropathy.

Kidney transplantation in young children: should there be a minimum age?

The optimal age for transplantation in children with ESRD remains controversial. The size of the recipient is important because successful transplantation requires adequate perfusion of the transplanted organ. Most centers loosely adhere to a lower weight limit of 10 kg, but a study by Humar A et al[93] reported an improved RT and graft survival in children < one year at the University of Minnesota.

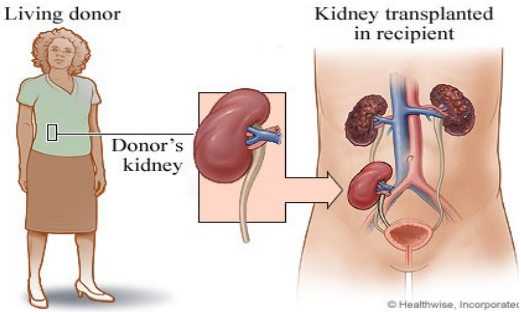


Figure 30- Living Kidney transplant (www.healthlinkbc.ca).

Kidney transplantation is very expensive, but it is a cost-effective treatment for children with ESRD with improved quality of life of the recipients. However, to avert organ rejection, the recipient must continue on life-long immunosuppressive therapy.

Although KT can avoid the need for dialysis, it is necessary to have access to dialysis incase complications develop leading to graft non-function. Preemptive KT where kidney transplant is

done straight away without dialysis is recommended as the best treatment where feasible, as it offers a significant allograft survival. It minimizes the CKD associated morbidity and dialysis related complications. Preemptive KT may not be possible in developing countries due to late presentation of CKD patients, and high cost of KT.

RRT are not truly "cures" for kidney disease, but a successful kidney transplant will improve life expectancy and quality of life of the patients, though with lifelong immunosuppressive drugs.

In Nigeria, there are up to 15 Government and private health facilities that do KT, but only 3 centers have transplanted children, and there are no existing transplant registries. These centers do only living related donor transplant and none offers deceased transplant.[92] Kidney transplant has not commenced in UPTH but we provide care to children after successful kidney transplant done in other hospitals. In our studies, we found that medical students and health workers had negative attitude towards organ donation on demise which would adversely affect deceased transplant programme in Nigeria .[94,95]

CHALLENGES IN THE CARE.

We encounter numerous challenges in the care of children with kidney diseases in Nigeria, which impact negatively on our patients and may lead to disease progression to ESRD and death. These include;

1. Delayed/Late presentation- The reasons include poverty, ignorance, lack of transportation which restrict access to care, poor health seeking behaviour or delayed referral.[96-98] In developed countries virtually all patients with CAKUT especially PUV, a common cause of CKD are diagnosed in-utero, whereas prenatal diagnosis is less than 10% in Nigeria resulting in presentation at late infancy, adolescents or second

decade of life.[71,96,97] In our study delayed presentation (58.8%) was associated with high mortality among patients with AKI in UPTH.[29] There is knowledge gap in renal care among doctors as seen in the practice of renal biopsy in Port Harcourt which may cause delay referral to Paediatric Nephrologists.[99]

2. Poverty- In 2013 estimate by the United Nations, 10.7 percent of the world's populations were living below the International poverty line of $1.90 a day. Nigeria has been named the poverty capital of the world according to World Poverty Clock (Figure 30). Out of estimated 180 million population of individuals in Nigeria, 86.9 million (48.3%) are living in extreme poverty.[100]

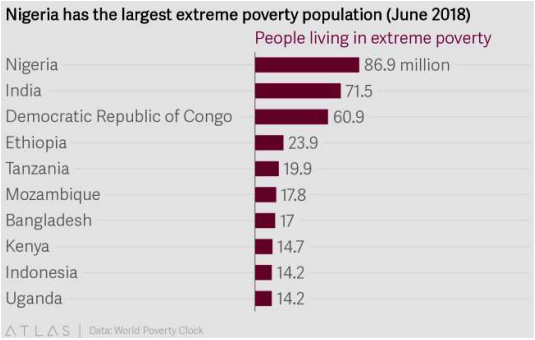


Figure 30-Poverty level of countries including Nigeria (www.qz.com)

Poverty may predispose to illness, affect the health seeking behaviour of parents, drug affordability, access and choice of treatment. A review of HD across the country showed that most ESRD patients cannot sustain 3 times per week HD; and by the end of a three month period, majority(over 90%) had stopped HD due to lack of funds.[98]

3. **Cultural/Traditional beliefs-** The patronage of traditional healers, belief that diseases are caused by evil spirit and the use/abuse of herbal concoctions which are harmful to the kidneys apparent in Nigeria delay seeking orthodox medical treatment until disease is well advanced. Unfortunately, this belief system holds irrespective of the educational level as demonstrated in our study where 39.3% medical students would refuse voluntary kidney donation due to traditional belief of re-incarnating without the donated kidney, even among some health workers.[94,95]

4. High cost of Medical services- The cost of medical services including drugs for kidney care is exorbitant in Nigeria in spite high level of poverty. A bottle of 20% Albumin infusion cost N65, 000(178USD)/ 100ml, Haemodialysis- N25-30,000 (65-82USD) per session, 2liter bag of PD fluid- N5,000 , Tenckoff catheter N10-15,000 , N17-20,000 for biopsy gun etc. The comparative cost of PD and HD for AKI depends on the weight of the child, and duration of dialysis.[101] The equipment and consumables including PD fluids and accessories are mostly imported and may account for high cost of kidney care. KT costs between N7.1 to 10million (22,500-27,778USD) excluding the cost of daily immunosuppressive therapy. Due to the high cost of treatment, patients are unable to purchase the prescribed drugs, commence and sustain dialysis when indicated. In a review of PD in children with AKI done in UPTH, dialysis access rate was very low (24.1%) due to unavailability of PD materials and poverty, with resultant high mortality rate among our patients.[88]

5. Counterfeit and Fake drugs- There is high prevalence of fake drugs reported in the West African sub-region including Nigeria.[102] The uninhibited sale and distribution of these adulterated, banned, fake drugs in open markets and without registration contribute to kidney damage in children, as seen

during “My pikin” epidemics in Nigeria in 2008, and may worsen kidney disease.

6. Poor Health Facilities- The infrastructure in most hospitals is substandard with lack of modern diagnostic equipment and constant power outages. There are sub-optimal laboratory services with delays in obtaining results, unavailability of Electron microscopy (EM) and Immunofluorescence microscopy (IM) for analysis of renal tissues, limited radiologic services and restricted pharmaceutical services. There is inadequate staffing with limited manpower like paediatric renal nurses, dieticians, psychologists, play therapists, social workers to manage children with kidney diseases. There are only 55 Paediatric Nephrologists serving 72-80million population of children in Nigeria.

7. Lack of Government subsidy- In Nigeria, the enormous financial burden on the care of children with kidney diseases is borne by parents/ guardian who pay out of pocket, with limited government support. In developed countries especially USA, Canada and United Kingdom the cost of kidney care including dialysis and KT is covered by Medicare or Medical Insurance, as such free for patients.[103]

The National Health Insurance Scheme (NHIS) established under Act 35 of 1999 by the Federal Government does not provide effective coverage for kidney care in children and no coverage for KT. More recently, NHIS made provision for only six sessions of haemodialysis for patients but this is very inadequate for patients with CKD.[104] **Therefore, almost all children (>90%) with ESRD in Nigeria die within few years of diagnosis due to inability to afford dialysis or KT, thus making CKD a “death sentence”.**

PREVENTION

In view of the numerous challenges in the care of children with kidney diseases, and the fact that CKD has no cure, I conclude that prevention of kidney disease is the "**CARE BEYOND CURE**". This can be achieved using the five levels of prevention;

1. General Health Promotion

This entails public health enlightenment, environment sanitation to control pollutions and infections, provision of good housing with prevention of overcrowding, as well as clean water supply, through the implementation of the 17 Sustainable Development Goals (SDGs).[103,105]

2. Specific protection

These are measures directed at combating predisposing factors to kidney diseases such as protecting against diarrhea(Rotavirus vaccine, breastfeeding, good handwashing etc) , HIV infection (PMTCT), malaria [106,107] (insecticide treated bed net, window net etc) , UTI (good toilet hygiene, regular voiding, avoidance of constipation etc), low birth weight, birth asphyxia, preterm birth (good maternal health & antenatal care), Obesity (lifestyle changes), Hepatitis B (HB vaccination), restriction on the sale and use of nephrotoxic drugs such as NSAIDs, herbal concoctions and bleaching cream, and adequate fluid intake to ensure good hydration and urination.

Increase public awareness by educating the populace about kidney health, how to avoid predisposing factors, and to dispel some cultural practices that promote kidney diseases through activities of the Nephrologists as seen during the World Kidney Day celebration.

3. Early diagnosis and prompt treatment

This requires a high index of suspicion and screening for early detection of kidney diseases in children and in foetuses who are not "weeing" in the womb. **The "search" for urine in children before and after birth is an important aspect of prevention of kidney disease, and informs the choice of the title of this inaugural lecture.**

Mass screening of well children by performing routine dipstick urinalysis, measurement of blood pressure and body mass index for early detection of kidney diseases, and risks factors of CKD such as proteinuria, haematuria, hypertension and obesity. We have identified and followed up children with risk factors of CKD found during the WKD activities and during epidemiologic studies at UPTH. [108-113]

Prompt referral of children with reduced urine output, and suspected kidney disease to facilities with Nephrologists for treatment is crucial for improve outcome. Availability of creatinine point-of-care (POC) testing will also facilitate prompt diagnosis of kidney disease, and follow up of patients.

4. Limitation of Disability

This include control of modifiable risk factors such as proteinuria, hypertension with angiotensin-converting enzyme inhibitors (ACEI) or angiotensin-receptor blockers (ARB), and anaemia with recombinant erythropoietin, and provision of renal replacement therapy.

5. Rehabilitation-

It involves kidney transplantation and the management of other co-morbidities associated with ESRD**.** Unfortunately, this level of prevention is not affordable for our patients.

As I draw close to the end of my lecture, I want to inform the audience of the preventive strategies the Nephrology Community in UPH/UPTH has put in place to ensure

sustenance of the kidney care in our hospital and in Nigeria in general.

The Paediatric Nephrology Unit has sister renal center (SRC) programme with Children's Hospital at Montefiore, New York, courtesy of the effort of our mentor Prof Felicia Eke, while the Adult Nephrology Unit has SRC with Salford Royal Hospital, Manchester. This would enable continuous exchange of knowledge and improvement in skills through the assistance of our Supporting Centers abroad.

We partner with the International Society of Nephrology (ISN) and International Paediatric Nephrology Association (IPNA) who assist us in increasing awareness of kidney diseases to the populace, through WKD activities, sponsoring of Ambassadorial programmes, Teaching Courses, Sister-renal center (SRC) programme and Fellowship training of young residents.

Our Nephrology associations such as African Paediatric Nephrology Association (AFPNA), Nigerian Association of Nephrologists (NAN) and Paediatric Nephrology Association of Nigeria (PNAN) are actively involved in enhancing kidney care in Nigeria. We also have an association with Rekiff Kidney Foundation, a non-governmental organization who provides financial assistance to our patients as well as sponsor some of our activities like public health enlightenment and screening of the communities for risk factors of CKD.

RECOMMENDATIONS

Government and NGO roles

a. Government should ensure implementation and achievement of the SDGs especially goals 1, 3 and 6. They should create enabling environment and job opportunities to eradicate poverty, provide clean environment devoid of infections and pollutants that predispose to kidney diseases, enforce strict regulation on the sale of nephrotoxic drugs like NSAIDs, counterfeit drugs and traditional medicine; provide Universal health coverage including wide immunization coverage against Hepatitis B infection, and availability of Rotavirus vaccine for control of diarrhoea.

b. Government should upgrade the Health facilities to provide effective kidney care at an affordable cost or free of charge for children. They should enforce legislation reducing the cost of dialysis by promoting local production of PD fluid and dialysis supplies. Government should scale up the National Health Insurance Scheme (NHIS) to cover for the treatment of kidney diseases in children including kidney transplantation.

c. The non–governmental organizations (NGO) should support Government to promote community kidney health awareness, and improve routine screening of apparently healthy children (asymptomatic) as part of School Health Programme during pre-school, primary and secondary schools entry for early detection of risks factors of CKD.

Health Workers' roles

a. Health workers must do routine dipstick urinalysis on every sick child who comes to the Health Facility.

b. Children with risk factors of CKD such as proteinuria, haematuria and Hypertension, and those with reduce urine output should be referred early by health workers to the Nephrologists for prompt treatment.

c. Health workers should encourage routine prenatal ultrasonography of every pregnant woman at 12-14weeks, 20weeks and 32weeks gestation by experienced radiologists for early detection of babies with CAKUT who are not weeing in the womb, and inform Paediatric Nephrologists /Urologists.

d. Health workers must observe and document the urinary stream of every male newborn baby within 48 hours of life, and refer those with abnormal stream to Nephrologists/Urologists.

e. Health workers should participate in massive health campaign on the prevention of kidney diseases, and regular screening of the community for urine abnormalities, hypertension and obesity. This health talk includes encouraging pregnant women to attend antenatal care and to deliver in health facilities.

f. They should provide prompt and proper treatment of sore throat and skin rashes to avoid kidney disease.

Individual roles

a. Pregnant women should book for antenatal care early in pregnancy, and deliver in a Health Facilities with trained mid-wives and Obstetricians, to prevent preterm births, birth asphyxia and low birth weight babies. They should avoid patronizing untrained traditional birth attendants, and consumption of local herbs.

b. Parents and caregivers should avoid giving non-prescribed medications to their children especially NSAIDs (Ibuprofen, Cataflam) or herbal concoctions as they damage the kidneys.

c. Lifestyle modification such as regular physical exercise and dietary control should be encouraged for healthy living and control of obesity.

d. Parents and caregivers should observe the urine stream of their newborn males within 48hours of life and present to hospital immediately if abnormal.

e. Parents should monitor the urine of their young children in terms of colour, and quantity especially when they have fever, vomiting or diarrhea etc for early identification of AKI, and refer promptly to health facilities. Older children are also recommended to observe their urine.

f. Parents and caregivers should give enough water to their children, such as 1-2L of water/day if >one year to maintain effective urination, avoid constipation, wipe females from front to back, and encourage them to void regularly to avoid urinary tract infection.

CONCLUSION

Urine is valuable, informative and has a secret language. The "Search" for urine is the beginning of kidney care.

**A*ccording to late Chinua Achebe "A man who calls his kinsmen to a feast does not do so to save them from starving. They all have food in their homes. When we gather together in the moonlit village ground it is not because of the moon. Every man can see it in his own compound; we come together because it is good for kinsmen to do so*".

It is indeed good that we are gathered together to listen to this lecture, not because we don't know about urine, but for us to pay attention to the urine of our children, and understand its secret language, in order to prevent CKD which has no cure.
Mr Vice-Chancellor Sir, Permit me to share this POEM**.**

THE SECRET LANGUAGE OF URINE.

Each body fluid is a language in which diseases speak to physicians
Urine speaks a unique language by its presence or absence
Valuable as gold
Sought after even in the darkness of the womb
A Nephrologist would turn a urine sample into a diagnosis.
I recall carrying a small, plastic urine cup to the side laboratory behind Prof Felicia Eke
She plunged a dipstick into the urine to reveal that unseen by the naked eye.
She placed some urine into a centrifuge, which spun rapidly
After peering through a microscope at a single drop of the urine
The diagnosis turned out to be Urinary tract Infection
And the urine culture confirms the diagnosis
From that moment, I was determined to learn and comprehend urine's subtle language.
Urine is more than a handy diagnostic body fluid — it keeps us human.
(Modified Excerpts by Jonathan Reisman, 2016. *outlook@washpost.com*)

I wish to end my lecture by **Echoing Martin Luther King Jnr's speech, hereby modified;**
"*I have a dream that one day this country will rise up and support kidney care in children; that one day our children will live and grow in an environment devoid of risks of kidney diseases.*
I have a dream that one day children with risks of kidney diseases will be identified early as we search for urine, and be treated free of charge.
***I have a dream that one day no child anywhere in this country will die from kidney disease, and there will be a cure for CKD*". I have a dream!**

Thank you for listening.

REFERENCES

1. Convention on the Rights of the Child. Office of the High Commissioner for Human Right. Archived from the Original on 13th January 2015.
2. Ibadin MO. The Genito-urinary System in Azubuike JC, Nkanginieme K E. Paediatrics and Child Health in a Tropical Region, 2nd edition, African Educational Press, Nigeria 2007; 469-75.
3. Anatomy and Physiology II. www.courses.lumenlearning.com/suny_ap2/chapter/ Physiology- of- urine- formation.
4. Sandler TW. Urogenital system. In Langman Medical Microbiology, 10th Edition, Lippincott, Williams and Wilkins 2006:322-325.
5. Langman's Medical Embryology 10th Edition. Lippincott reverend & adventurer, 2006, 37. ISBN / ASIN: 0781794854
6. Glassberg KI. Normal and abnormal development of the kidney: a clinician's interpretation of current knowledge. J Urol 2002; 167:23-39.
7. https://www.boundless.com/physiology/textbooks/boundless-anatomy-and-physiology-textbook/urinary-system-25/urine-transport-storage-and-elimination-242/micturition-and-the-micturition-reflex-1186-11136/
8. Koff S.A . Estimating bladder capacity in children. Urology.1983;21 :248.
9. Madormo C. Normal urinary Frequency per Day for Children. www.livestroong.com/article/269579-normal-urinary-frequency-per-day-for-children.
10. Singla D, Malik P, Sangwan M, Garg MK. Age, gender, and voided volume dependency of peak urinary flow rate and uroflowmetry nomogram in a tertiary care centre. Asian Pac J Health Sci., 2018; 5:13-16.

11. Drach GW, Ignatoff J, Layton T. Peak urinary flow rate: Observation in female subjects and comparision to male subjects. J Urol 1979;122 :215-9.
12. https://www.introducingbrussels.com/manneken-pis
13. https://forum.facmedicine.com/threads/what-your-urine-is-telling-you-about-your-health.
14. Prasad Devarajan. Acute Kidney Injury. In Chand D H, Valentini R P(eds). Clinician's Manual of Pediatric Nephrology 2011, World Scientific Publishing Co, Singapore, 437-464.
15. Hui WF, Chan WK, Miu TY. Acute kidney injury in the paediatric intensive care unit: identification by modified RIFLE criteria. Hong Kong Med J 2013; 19:13-9.
16. Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Crit Care 2007;11:R31.
17. Acute Kidney Injury Work Group. Kidney Disease: Improving Global Outcomes (KDIGO) - Clinical Practice Guideline for Acute Kidney Injury. Kidney Int 2012;2 :1-138.
18. **Anochie I C**. Diarrhoea: a prelude to acute renal failure? Afr Health 2004,3
19. Halle MP, Lapsap CT, Barla E, Fouda H, Djantio H, Moudze BK et al **.** Epidemiology and outcomes of children with renal failure in the pediatric ward of a tertiary hospital in Cameroon. BMC Pediatrics 2017; 17: 202
20. Amal Bourquia, Felicia Eke**, Ifeoma Anochie**. Acute renal failure in limited resource country. In African Paediatric Nephrology Guidebook 2015: 185-204
21. Eke FU, Eke NN. Renal disorders in children ; A Nigerian Study. Paed Nephrol 1994;8 :383-386.

22. Onifade, EU. A 10 -year review of childhood renal admissions into Lagos University Teaching Hospital , Nigeria. Nig Q J Hosp Med 2003; 13:3-4.
23. Olowu, W. A. Paediatric acute renal failure in South Western Nigeria. Kidney Int; 2004; 66:1541-8.
24. Ibadin OM , Ofovwe EG. Pattern of renal diseases in children in Midwestern zone of Nigeria. Saudi J Kidney Dis Transpl. 2003; 14:39-44.
25. Etuk IS, Anah MU, Ochigho SO, Eyong M. Pattern of paediatric renal disease in inpatients in Calabar, Nigeria. Trop Dr. 2006; 36:256.
26. Ikpeme, E. E. & Dixon-Umo, O.T.Paediatric renal diseases in Uyo, Nigeria: a 10- year review. Afr J. Paed Nephrol 2014; 1:12-17.
27. Ocheke, I. E., Okolo, S. N., Bode- Thomas, F. & Agaba, E. I. Pattern of childhood renal diseases in Jos, Nigeria. A preliminary report. J Med Trop 2010;12:52-53
28. Okoro BA, Okafor HU. Pattern of childhood renal disorders in Enugu. Nig J Paed 1999; 26:14-18.
29. **Anochie I C,** Eke FU. Acute renal failure in Nigerian children: Port Harcourt experience. Paed Nephrol 2005; 20:1610-1614.
30. Anigilaje EA, Adesina TC. The pattern and outcomes of childhood renal diseases at University of Abuja Teaching Hospital, Abuja, Nigeria: A 4 year retrospective review. Nig Postgrad Med J 2019;26:53-60
31. Okafor HU, Okoro BA, Ugwu GI. Acute glomerulonephritis in Enugu. Nig J Paed 1995;22:31-5.
32. **Anochie I C**, Eke F U, Okpere A N. Childhood Acute Glomerulonephritis in Port Harcourt,Rivers State, Nigeria. Nig J Med 2009; 18: 162-167.
33. **Anochie IC**, Eke FU, Okpere AU. Complications of acute Glomerulonephritis in children in Port Harcourt . Nig J Paed 2008; 35:7-11.

34. Shahrbaf F G, Assadi F. Drug-induced renal disorders. J Renal Inj Prev 2015; 4:57-60.
35. H. O. Okuonghae, I. S. Ighogboja, J. O. Lawson & E. J. C. Nwana. Diethylene glycol poisoning in Nigerian children, Ann Trop Paed 1992; 12: 235-238.
36. Litovitz TL, Klein-Schwartz W, Dyer KS, Shannon M, Lee S, Powers M. 1997 annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. Am J Emerg Med 1998; 16:443–97.
37. Akuse RM, Eke FU, Ademola AD, Fajolu IB, Gbelee HO, Ihejiahi U, Bugaje M, **Anochie IC** et al. Diagnosing renal failure due to diethylene glycol in children in a resource-constrained setting. Paed Nephrol 2012, DOI: 10.1007/s00467-011-2082-8.
38. **Anochie I**. Enuresis. Nig J Clinic Pract 2003; 6:111-114.
39. Ritting S, Kamperis K. Pathophysiology of nocturnal enuresis. In Franco I, Austin PF, Bauer SB, von Gontard A, Homsy Y. Pediatric incontinence: Evaluation and clinical management. John Wiley & Sons, Ltd, 2015: 207-219
40. **Anochie I C**, Ikpeme E E. Nocturnal enuresis among secondary school students in Port Harcourt. Port Harcourt Med J 2006; 1:12-16
41. Paul NI, Alikor EAD, **Anochie IC.** Prevalence of enuresis among primary school children in Port Harcourt. Nig J Paed 2012; 39:18-21
42. Paul NI,Alikor EAD,**Anochie IC**. Factors associated with enuresis among primary school children in Port Harcourt. Nig J Paed 2013; 40: 370-374
43. Wald ER. Cystitis and pyelonephritis. In: Feigin and Cherry's Textbook of Pediatric Infectious Diseases, 8th ed, Cherry JD, Harrison G, Kaplan SL, et al (Eds), Elsevier, Philadelphia 2018. p.395.

44. Jakobsson B. Berg U. Svensson L. Renal scarring after acute pyelonephritis. Arch Dis Child 1994; 70:111-115.
45. **Anochie I. C.**, Nkanginieme K. E. O., Eke F. U. Urinary Tract Infection; The influence of Instruction on method of urine collection and storage. Nig J Paed 2001; 28: 39-42
46. Woroniecki R. P., Becknell B, Smoyer W. E. Steroid Sensitive and Steroid Resistant Nephrotic Syndrome. In Chand DH, Valentini RP. Clinician's Manual of Pediatric Nephrology, World Scientific Publishing Co, Singapore 2011, 175-200.
47. Ugwu GM. Childhood Nephrotic syndrome in Oghala, Delta State. Afr J Paed Nephrol 2014 ;1:2-7.
48. Adedoyin OT, Adesiyun OO, Mark F, Anigilaje EA, Adeniyi A. Congenital nephrotic syndrome in a Nigerian child. Nig J Paed 2006; 33: 109-112.
49. Adekanmbi AF, Ogunfowora OB, Ogunlesi TA, Ogundeyi M. M., Olowu AO, Sotimehin S.A . Congenital nephrotic syndrome in a Nigerian infant. J Trop Pediatr 2007; 53:287-291.
50. A. N. Okpere , **I.C Anochie** , F.U Eke. A case report of Infantile Nephrotic syndrome in Port Harcourt: Challenges of Management and review of literature. Afr J Paed Nephrol 2015; 2: 13-17.
51. Hendrickse RG, Gilles HM. The nephrotic syndrome and other renal diseases in children in Western Nigeria. East Afr Med J 1963; 40:186-201.
52. Eke *FU.* Nephrotic syndrome in Port Harcourt –clinical presentation and response to steroids. Nig J Pediatr *1990*; 17:59–63.
53. Abdurrahman MB, Aikhionbare HA, Babaoye FA, Sathiakumar N, Narayana PT. Clinicopathological features of childhood nephrotic syndrome in northern Nigeria. Q J Med. 1990 ;75:563-76.

54. Asinobi AO, Gbadegesin RA, Adeyemo A A. The predominance of membranoproliferative glomerulonephritis in childhood nephritic syndrome in Ibadan, Nigeria. West Afr J Med 1999; 18:203-206.
55. Okoro BA, Okafor HU, Nnoli LU. Childhood nephrotic syndrome in Enugu, Nigeria. West Afr J Med. 2000;19:137–141
56. Adedoyin OT, Gbelee HOD, Adeniyi A. Childhood nephrotic syndrome in Ilorin. Nig J Paed 2001: 28; 68-72.
57. Fanconi G, Kousmine C, Frischknecht W. Die konstitutionelle Bereitschaft zum Nephrose syndrom. Helv Paediatr Acta.1951;6:199-218
58. Dummer PD, Limou S, Rosenberg A Z, Heymann J, Nelson G, Winkler C A, Kopp J B. APOL1 Kidney disease risk variants-an evolving landscape. Semin Nephrol. 2015; 35: 222–236.
59. **Anochie IC**, Eke FU, Okpere AN. Familial FSGS in a Nigerian family and exclusion of mutations in NPHS2, WT1 AND APOL1. West Afr J Med 2012;31:273-276
60. Gipson DS, Massenill SF, Yao L. Management of childhood onset nephrotic syndrome. Pediatrics 2009; 124-127.
61. **Anochie IC**, Eke FU, Okpere AN. Childhood Nephrotic syndrome: change in pattern and response to steroid. J Natl Med Assoc 2006; 98: 1977-1981.
62. **Anochie IC**, Okpere AN, Eke FU. Childhood Idiopathic Steroid Resistant Nephrotic Syndrome in Southern Nigeria. Afr J Paed Nephrol 2014; 1:18-24.
63. Trautmann A, Schnaidt S, Lipska-Ziętkiewicz B S, Bodria M, Ozaltin F, Emma F et al. Long-Term Outcome of Steroid-Resistant Nephrotic Syndrome in Children. J Am Soc Nephrol 2017; 28:3055–3065.

64. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 2002; 39:S1.
65. Odubanjo MO, Okolo CA, Oluwasola AO, Arije A. End-stage renal disease in Nigeria: an overview of the epidemiology and the pathogenetic mechanisms. Saudi J Kidney Dis Transpl. 2011;22:1064-71
66. Harambat J,va Stralen KJ, Kim JJ, Tizard EJ. Epidemiology of chronic Kidney disease in children. Pediatr Nephrol 2012; 27:363-373.
67. **Anochie I C**, Eke F U. Chronic renal failure in children; a report from Port Harcourt, Nigeria. Pediatr Nephrol 2003; 18:692-695.
68. **Anochie I C**, Eke F U. Obstructive uropathy in childhood, as seen in the University of Port Harcourt Teaching Hospital, Nigeria. Nig J Med 2004; 13:136-9.
69. **Anochie IC**, Nwosu S O. Obstructive uropathy in a Nigerian child due to bladder rhabdomyosarcoma. Niger Health J 2004; 3: 206-208.
70. Makrina Savvidou, H K Dhillon, Urinary Tract Abnormalities In Twining's Textbook of Fetal Abnormalities (Third Edition), Chapter 18, 2015:479-517.
71. Jaja T,**Anochie IC,** Eke FU. Prevalence of Posterior urethral valve in childhood in Port Harcourt. Port Harcourt Med J 2012; 6: 10-16.
72. Baggaley RF, Boily MC, White RG, Alary M. Risk of HIV-transmission for parenteral exposure and blood transfusion: a systematic review and meta-analysis. AIDS 2006; 20: 805-812.
73. **Anochie IC**, Eke FU, Okpere AN. HIV associated nephropathy in Nigerian children. Paed Nephrol 2008; 23:117-122.

74. Eke FU, **Anochie IC,** Okpere AN, Eneh AA, Ugwu RO, Ejilemele AA, Ugboma HU .Microalbuminuria in children with Human Immunodeficiency virus (HIV) Infection in Port Harcourt, Nigeria. Nig J Med 2010; 19: 298-301.
75. Okpere AN, **Anochie IC** , Eke FU , Bell-Gam HI, Jaja T . Risk factors of Chronic Kidney Disease in Secondary School Girls in Port Harcourt: A World Kidney Day activity. Port Harcourt Med J 2012 ;6: 407-415.
76. Eke F.U. The agony and the Ecstasy of Paediatric Nephrology. 5^{4th} Inaugural lecture series, University of Port Harcourt, 2006.
77. van der Watt G, Omar F, Brink A, McCulloch M: Laboratory Investigation of the Child with Suspected Renal Disease. In Pediatric Nephrology 7th ed., edited by Avner ED, Harmon WE, Niaudet P, Yoshikawa N, Emma F, Goldstein S, Heidelberg, Springer, 2016: 613-636
78. Patel HP. The Urinalysis. In Chand DH, Valentini R P (eds). In Clinician's Manual of Pediatric Nephrology. World Scientific Publishing Co. Singapore 2011: 9-19.
79. Eke G, **Anochie I C**, Eke F U. Dipstick urinalysis as a screening tool in the diagnosis of urinary tract infection in Children. Nig Med Pract 2010; 57:55-59
80. Ekeke ON, Eke N. Posterior Urethral valve: management in the resource-limited economies. Afr J Paed Nephrol 2014; 1:67-76.
81. Ingraham SE, Patel HP. Evaluation of Renal Function in the Pediatric Patient. In Chand DH, Valentini R P (eds). In Clinician's Manual of Pediatric Nephrology. World Scientific Publishing Co. Singapore 2011:20-36.
82. Mian AN, Schwartz GJ. Measurement and Estimation of GFR in children. Adv Chronic Kidney Dis 2017; 24:348-56.

83. Alexopolous E. How important is renal biopsy in the management of patients with glomerular diseases? Nephrol Dial Transplant 2001; 6:83-5.
84. Saudi Mendeliome Group. Comprehensive gene panels provide advantages over clinical exome sequencing for Mendelian diseases**.** Semin Nephrol 2015; 35: 222–236.
85. KDIGO Clinical Practice Guideline update for the diagnosis, Evaluation, prevention, and treatment of Chronic Kidney Disease-Mineral Bone disorder (CKD-MBD). Kidney Int Supp 2017;7:1-59.
86. Sutherland SM, Alexander SR. Continuous renal replacement therapy in children. Pediatr Nephrol 2012 ;27:2007-2016.
87. Segar WE,Gibson RK, Rhanny R. Peritoneal dialysis in infants & children .Pediatrics 1961; 27: 603-613
88. **Anochie I C**, Eke F U. Paediatric acute peritoneal dialysis in southern Nigeria. Postgrad Med J 2006; 82:228-230
89. Srisuwan K, Geary D.F. Pediatric Haemodialysis. In Chand DH, Valentini R P (eds). In Clinician's Manual of Pediatric Nephrology. World Scientific Publishing Co. Singapore 2011:507-521.
90. Keita Y, Ndongo AA, Engome CB, Sow NF, Seck N, Thiam L et al.Continuous ambulatory peritoneal dialysis (CAPD) in children: a successful case for a bright future in a developing country. Pan Afr Med J 2019. www.panafrican.med-journal.com
91. Milford D V. A practical approach to renal transplantation in children. Afr JPaed Nephrol 2016; 3 :84-91.
92. Okafor UH. Kidney Transplantation in Nigeria: a single center experience. Pan Afr Med J 2016. www.panafrican.med-journal.com

93. Humar A, Arrazola L, Mauer M, Matas AJ, Najarian JS. Kidney transplantation in young children: should there be a minimum age? Pediatr Nephrol. 2001; 16: 941-5.
94. **Anochie I C**, Ofori P. Attitude of medical students toward voluntary kidney donation. The Nig Hlth 2001; 2:175-176.
95. Okpere AN, **Anochie IC**. Knowledge and Attitude of Healthcare Workers towards Kidney Transplantation in Nigeria. Nig J Paed 2014; 41: 48-53.
96. Esezobor CI. The sorry state of Children with Kidney disease in Nigeria. The Lancent 2019.
97. Asinobi AO, Ademola AD, Ogunkunle OO, Mott SA. Paediatric end-stage renal disease in a tertiary hospital in South West Nigeria. BMC Nephrol 2014; 15: 25-29.
98. Agbaji O O, Abene EE. Care of patients with end-stage renal disease in Nigeria: a call for a change in paradigm. Jos J Med 2012; 16:28-31.
99. Obiorah CC, **Anochie I.C.** Knowledge, Attitude and Practice of Renal biopsy among Consultant Nephrologists and Senior Nephrology Residents. Afr J Paed Nephrol 2017; 4: 85-91.
100. Kazeem Y. Nigeria has the highest rate of extreme poverty. Quartz Africa 2018.
101. Obiagwu PN, Abdu A. Peritoneal dialysis vs Haemodialysis in the management of acute kidney injury in Kano, Nigeria: a cost analysis. Trop Med Int Health 2015; 20: 2-7
102. Akiny O. Counterfiet drugs in Nigeria: A threat to public health. Afr J Pharm Pharmacol 2013; 7:2571-2576.
103. Luyckx VA, Tonelli M, Stanifer JW. The global burden of kidney disease and the sustainable development goals. Bull WHO 2018; 96:414-422.

104. Obalum DC, Fiberesima F. Nigerian National Health Insurance Scheme: an overview. The Nig Post grad Med J 2012; 19:167-74.
105. United Nations: Transforming our world: The 2030 Agenda for sustainable development. Pages 1-36. www.sustainabledevelopment.un.org
106. Okpere AN**, Anochie I.C**, Eke F.U. Acute Kidney Injury in Children with severe malaria. Afr J Paed Nephrol 2017; 4: 28-33
107. Aiyedun C, Opara PI, **Anochie I.C**. pRIFLE and Prevalence of Acute Kidney Injury in under-five Children with severe malaria:Any Change?. Afr J Paed Nephrol 2017; 4: 72-78
108. Ugboma H A, Eke FU, **Anochie IC.** World Kidney Day Activities-A pilot study or the prevention of kidney diseases in Nigeria. www. Nephroprevention.org 2007.
109. Okpere AN, **Anochie IC**, Eke FU. Prevalence and risk factors of Microalbuminuria among secondary school children in Port Harcourt, Rivers State, Nigeria. Afr Hlth Sci 2012; 12: 140-147
110. Okpere AN, **Anochie IC**, Eke FU. Evaluation of Microalbuminuria in Obese Adolescents. Nig J Paed 2012; 39: 128-132.
111. Okpere AN, **Anochie IC**, Eke FU. Pattern of Blood pressure and hypertension in Adolescents in Port Harcourt, Nigeria. West Afr J Med 2013; 32:93-98.
112. Okagua Joyce, **Anochie Ifeoma**. Blood pressure Profile and Hypertension in Adolescents in Port Harcourt, Southern Nigeria. Afr J Paed Nephrol 2014; 1: 77-82
113. Okagua J, **Anochie IC**, Akani N A. Adolescent blood pressure pattern in Rivers State, Nigeria: A rural-urban comparison. Nig J Paed 2015; 42: 26-32.

PROF IFEOMA COMFORT ANOCHIE,
MB.BS (UNIBEN), FWACP.

Prof Ifeoma Comfort Anochie was born on the 28th May, 1966 to the family of Late Sir Felix Ogbonna and Lady Comfort Chinwe Nwankwo at Enugu, in Enugu State. Her parents were renowned Educationists from Nibo in Awka South Local Government Area of Anambra State. Ifeoma as commonly known is the second of four children and the first daughter of her parents.

Education- She started her education early in life at the age of 4, from just accompanying her mother to school to being enrolled into a regular stream as she was found to be very intelligent. She completed her primary education at Central School Umudioka, Dunukofia LGA, Anambra State in June 1976, and proceeded without delay to Girls' Secondary School, Onitsha where she obtained the best result in the West African School Certificate Examination in 1981.

She attended Federal School of Arts and Science, Suleja, Niger State (1981-1983). She made an impressive result in the Higher School Examination, and gained admission into the prestigious University of Benin, Edo State where she studied

Medicine (1983-1989), and qualified with a Bachelor of Medicine and Bachelor of Surgery (MB, BS).
Dr Anochie did her housemanship in the University of Port Harcourt Teaching Hospital (UPTH) (1990-1991), and the National Youth Service at Orogbum Health Center, Port Harcourt (1991-1992). Shortly after the NYSC, she commenced Residency training in the Department of Paediatrics, UPTH in 1993, and completed the programme with a Fellowship of West African College of Physicians (FWACP) in April 1998.

EMPLOYMENT AND ADMINISTRATIVE EXPERIENCES

She was appointed a Lecturer 1 in the Department of Paediatrics and Child Health, College of Health Sciences, University of Port Harcourt on the 2nd of August 1999, and an Honorary Consultant Paediatrician in UPTH on the 5th September 2000. She progressed rapidly from a Senior Lecturer in 2002, through Reader in 2006 to become a Professor of Paediatrics, College of Health Sciences on the 4th May, 2010.

She has held several administrative positions in both the University and UPTH; acting Head, Department of Paediatrics and Child Health, University of Port Harcourt (2007-2010), UPTH (2008- 2010), and the Director, MacArthur Clerking Skills Laboratory, a world class digital clinical skills center (2011 –till date).

ACADEMIC ACTIVITIES AND OTHER SERVICES

Prof Ifeoma Anochie established the Endocrinology unit in the Department of Paediatrics, UPTH since 2000, and due to her interest in “pee” she settled for Nephrology, under the tutelage of Professor Felicia Eke. She has also received Clinical Fellowship in Paediatric Nephrology both in United States of America and United Kingdom.

She has been involved in many academic activities in the University and the hospital, including teaching of both medical students and resident doctors. She has successfully supervised Part II dissertations of 20 medical doctors who are all Consultants except for two. She is a reviewer to many Local and International journals, and a pioneer Editor-in-Chief of a Nephrology journal- African Journal of Paediatric Nephrology (2009 till date).

She has served as a member of many committees in the University, a member of University Strategic Planning (2012), Quality Assurance and Quality Control, representing Faculty of Clinical Sciences (2011) etc. She is a member of Senate, University of Port Harcourt since December 2007. She belongs to many professional bodies such as Nigerian Medical Association, Medical and Dental Consultants Association of Nigeria (MDCAN), Nigerian Association of Nephrology (NAN), Paediatric Association of Nigeria (PAN), Paediatric Nephrology Association of Nigeria (PNAN), African Paediatric Nephrology Association (AFPNA), International Paediatric Nephrology Association (IPNA), International Society of Nephrology (ISN). Prof Anochie has been an IPNA Councillor since 2013 representing West African sub-region, where she is involved in advocacy for kidney health of Nigerian children in particular.

She serves as an external examiner to many Medical Schools within Nigeria and in Accra, Ghana, and an examiner for the West African Postgraduate Medical College. She has attended accreditation exercises in many Hospitals in Nigeria, and in Liberia. She has been Chairperson at Conferences especially the Annual Interventional Nephrology Skills training in Port Harcourt and Chairman of Scientific sub-committees. Prof Anochie has attended many workshops, courses, fellowship programmes in Paediatric Nephrology and Endocrinology,

Local and International Conferences where she presented many papers, posters and has been a resource person. She has won many awards including Silver Medal Award at the University of Benin Medical Students' Association (UBEMSA) High Jump in Jos (1987), and 2nd Prize paper Award at 10th Annual Conference on Prevention in Renal Disease (Nephroprevention) in Toronto, Canada (2011).

RESEARCH PUBLICATIONS

Prof Anochie is a prolific writer and a researcher. She has **80 scientific publications** in reputable journals and still counting, and contributed 9 chapters in books, covering General paediatrics, Paediatric Nephrology and Endocrinology. She is an Editor of Introduction to Clinical Medicine (ICM), and MacArthur Clinical Skills Laboratory Structure Clinical Clerking: Performance Checklists, Checkoffs and Video Models for History taking, General and Systems Physical Examination.

FAMILY LIFE AND EXTRACURRICULAR ACTIVITIES

She is married to HRM Engr. /Sir Ben Anochie, with three children; two Medical doctors and a Medical student. She is a devout Christian, a great cook, a sport lover and a good dancer. Ladies and Gentlemen, I present to you a very intelligent academic, a teacher per excellence, soft spoken with calm demeanor, silent achiever, very accommodating consultant, a great mentor who inspires and transforms her mentees/trainees, a motivator, meticulous researcher and physician, an advocate of kidney health in children, a loving and caring mother, "Ada diora nma", Professor Ifeoma Anochie to deliver the 166th Inaugural Lecture of the University of Port Harcourt.

Professor Ndowa E.S Lale,
Vice- Chancellor.