



SYNOPSIS: NEONATAL CHOLESTASIS

Akinbami FO

Department of Paediatrics, Niger-Delta University Teaching Hospital, Okolobiri,
Bayelsa State, Nigeria.

E-mail: kaytoks@yahoo.com

Introduction

Neonatal cholestasis (NC) is a group of rare disorders of impaired bile flow characterized by conjugated hyperbilirubinaemia in the newborn and young infant. NC is never physiological but rather, it is a sign of hepatobiliary and/or metabolic disorders, some of which might be fatal if not identified and treated rapidly.

Definitions

Cholestasis – Cholestasis is defined as an impairment in the excretion of bile, which can be caused by defects in intrahepatic production of bile, transmembrane transport of bile, or mechanical obstruction to bile flow.^{1,2} The biochemical features of cholestasis reflect the retention of components of bile in the serum (such as bilirubin, bile acids, and/or cholesterol).

Conjugated hyperbilirubinaemia- A serum conjugated/direct bilirubin level >1 mg/dL in combination with a total bilirubin of <5.0 mg/dL, or a conjugated /direct bilirubin fraction of >20% of the total, if total bilirubin is >5.0 mg/dL, indicates NC.¹⁻³ It is a laboratory diagnosis, almost always indicative of a hepatobiliary disorder.

Incidence of neonatal cholestasis

This is approximately 1 in 2,500 live births.

Causes of Neonatal Cholestasis

Often the aetiology is unknown. However, the aetiologies may be divided into two categories: extrahepatic and intrahepatic factors as follows:

1. Extrahepatic causes are mainly biliary atresia, choledochal cyst, spontaneous perforation of bile duct, and cholelithiasis.
2. Intrahepatic causes include neonatal infections, genetic (Alagille syndrome, α -1 antitrypsin deficiency) and inborn errors of metabolism (galactosaemia, tyrosinaemia, fructosaemia), and progressive familial intrahepatic cholestasis (PFIC).

Causes of Cholestasis can also be classified into:

1. biliary (obstructive, large extrahepatic, or small intrahepatic bile ducts) or
2. hepatocellular (defect in membrane transport, embryogenesis, or metabolic dysfunction) in origin (Table I).

Of the various conditions that can present with NC, biliary atresia (BA) represents the major cause and has been reported to occur in 35–41%² of the cases followed by progressive familial intrahepatic cholestasis (PFIC) (10%), preterm birth (10%), metabolic and endocrinological disorders (9–17%), Alagille syndrome (ALGS) (2–6%), infectious diseases (1–9%), mitochondriopathy (2%), biliary sludge (2%), and, finally, idiopathic cases (13–30%).

Pathophysiology

The primary failure is of bile excretion → excess conjugated bilirubin in the blood and decreased bile salts in gastrointestinal tract. Inadequate bile in the GI tract → malabsorption of fat and fat-soluble vitamins (ADEK) → deficiency of vitamins ADEK, inadequate nutrition and growth failure.

Clinical manifestations of NC

Infants with cholestasis often have jaundice indistinguishable from that of infants with indirect hyperbilirubinaemia; the presence of pale stools, dark yellow urine or hepatomegaly, should suggest cholestasis. Acholic stool signifies biliary obstruction and should warrant further evaluation. Clinical manifestation of NC can be approached as follows:

Early presentation - Persistent jaundice from early weeks of life; passage of dark urine (due to conjugated bilirubin); acholic stool (triad of symptoms) and hepatomegaly.

Late presentation - Persistence of the cholestasis will lead to chronic pruritus, symptoms of fat-

soluble vitamins (ADEK) deficiency and growth failure. It will also lead to the development of hepatic fibrosis and cirrhosis which will manifest

with features of portal hypertension and subsequent, abdominal distension, ascites, dilated anterior abdominal wall veins and gastrointestinal bleeding.

Table I: Aetiology of neonatal cholestasis

<i>Disease Group</i>	<i>Category</i>	<i>Causes</i>
Hepatocellular	Neonatal hepatitis	TORCHES, Sepsis, UTI, Idiopathic neonatal hepatitis syndrome
	Metabolic	Inborn errors of metabolism (Galactosaemia, Tyrosinaemia, Fructosaemia), A1AT deficiency, Storage disorders
	Others, genetic, endocrine	PFIC, Hypothyroidism, Hypopituitarism, Trisomies, Polycystic disease
	Toxin	Total Parenteral Nutrition
Ductal (Obstructive)	Extrahepatic	Biliary atresia, Choledochal cyst, Spontaneous perforation of bile duct, Stone, Sludge
	Intrahepatic	Alagille syndrome, Non-syndromic biliary hypoplasia

UTI - Urinary Tract Infection; A1AT - α -1 Antitrypsin Deficiency; PFIC - Progressive Familial Intrahepatic Cholestasis

** Hepatotropic viruses A, B and C, in general, do not cause neonatal cholestasis. Therefore, specific studies for these infectious agents in the evaluation of NC are generally unwarranted.

Diagnostic Evaluation

Cholestasis is generally evaluated by obtaining a detailed history and a thorough physical examination. The current approach for evaluating an infant with NC, focuses on initially excluding BA,

following the red flags that indicate the likelihood of a specific aetiology (e.g extrahepatic features of ALGS) (Figure 1) and searching for other treatable conditions.^{2,3} (Table II)

Table II: Red flag findings for NC in history and on physical examination^{2,3}

<i>Red flags</i>	<i>Diseases to consider</i>
Maternal history (ANC)	
Prenatal Ultrasound abnormality	-Choledochal cyst, cystic biliary atresia, gallstone
Intrahepatic cholestasis of pregnancy	-PFIC
Maternal infection during pregnancy	-Congenital infections
Physical examination	
Acholic stool	-BA, Choledochal cyst, Biliary sludge/stone
Palpable mass in right upper quadrant	-Choledochal cyst
Ascites	-Spontaneous perforation of the bile duct
Heart murmur, skeletal abnormality (butterfly vertebrae, short ulna), posterior embryotoxon	-Alagille syndrome
Dysmorphic facies	-Alagille syndrome, chromosomal abnormality
Microcephaly, cataract, vision abnormalities,	-TORCH infections, Galactosaemia
Neurological abnormalities (irritability, lethargy poor feeding), hypotonia, seizures	- Metabolic and Mitochondrial disorders, sepsis,
Family history	
Early emphysema	-Alpha -1-antitrypsin deficiency
Liver disease in siblings or history of stillbirth	-Genetic disease or inborn error of metabolism
Consanguinity	-Autosomal recessive genetic liver disease

A critical and important initial blood test, is the measurement of the serum conjugated bilirubin which if elevated as earlier stated, is a reliable indicator of cholestasis and should be followed by

standard biochemical and synthetic liver function tests. Other laboratory tests that will help define the aetiology, the severity of liver disease and detect treatable conditions are listed in Table III.

Table III: Investigation of the persistently cholestatic infant

Organ/Tissue	Specific investigations
Blood	Initial Blood- FBC +diff, PT, APTT, INR, Liver function test (ALT, AST, AP, GGT, Total/Conjugated bilirubin), Albumin, Glucose, α -1-antitrypsin phenotype (Pi typing) and TSH, and T ₄ ; Complete metabolic screen for galactosaemia (RBC galactose -1-P uridyl transferase), Tyrosinaemia, Hypothyroidism; JAGGED testing for Alagille syndrome; Total serum bile acid level. Subsequently - serum amino acid assay, urine for organic acids assay; Bacterial culture if infant is clinically ill.
Urine	Chemistry, culture, reducing substances, Bile acid level for disorders of bile acid synthesis,
Imaging	Abdominal USS should be part of initial evaluation to assess for liver size, position, spleen size and number, ascites, choledochal cyst, gallstones, and bile sludge.
Hepatobiliary	Hepatobiliary scintigraphy with Technetium -labelled iminodiacetic acid analogue (HIDA) to assess biliary tract patency and rule out BA but specificity is low (30% to 80%).Cholangiography (intraoperative cholangiography [IOC]) remains the definitive diagnostic test for BA.
Liver	Liver biopsy remains the cornerstone of diagnostic workup of infants with NC (predictive accuracy for BA ranges from 85%-95%). Histological features include portal bile duct plugs, ductal reaction and portal fibrosis. Liver biopsy can also be helpful in establishing other causes of NC, including: A1-AT deficiency (intrahepatocytic globules) Alagille syndrome (bile duct paucity) Neonatal sclerosing cholangitis (necroinflammatory duct lesions) Viral infections (CMV or herpes simplex virus inclusions) Metabolic liver diseases (steatosis and pseudoacinar formation of hepatocytes) PFIC and other storage disease (electron microscopy findings)Idiopathic neonatal hepatitis (multinuclear giant cells, extramedullary haematopoiesis, hepatocellular cholestasis)

Management

All infants with NC, require careful attention to their nutrition, growth and vitamin levels. The management can be divided into general/supportive and specific treatment:

(a) Supportive

- Nutrition- oral feeding is preferred or parenterally, when oral feeding is not feasible.

-High calorie, protein feed viz -breast milk and MCT containing formula.

-Vitamins (ADEK) supplementation and monitor their levels.

-Administration of live vaccines.

-Anti-pruritic agents-Ursodeoxycholic acid (UDCA), \pm cholestyramine \pm rifampicin.

(b) Specific

- PFIC or ALGS (without cirrhosis or portal hypertension) - partial biliary surgical diversion, improves itching and cholestasis.

-Bacterial infection- antimicrobials.

-Metabolic - Dietary e.g galactose-free milk.

-BA- Hepatopertoenterostomy (HPE) best performed before 30-45 days of life. Bile drainage achieved in 90% if surgery is done within 2 months of age, and 20% after 90 days.⁴

Prevention

- Early Screening for infants with BA
- Stool colour screening system: infant stool colour card, given to caregiver to take home, document pale colour stools and bring back at one-month Well-Baby Clinic visit⁹
- Serum direct bilirubin level before discharge from hospital (usually elevated within 72 hours in BA)^{6,7}
- Novel markers- measurement of serum matrix metalloproteinase7(MMP7)^{1,8}

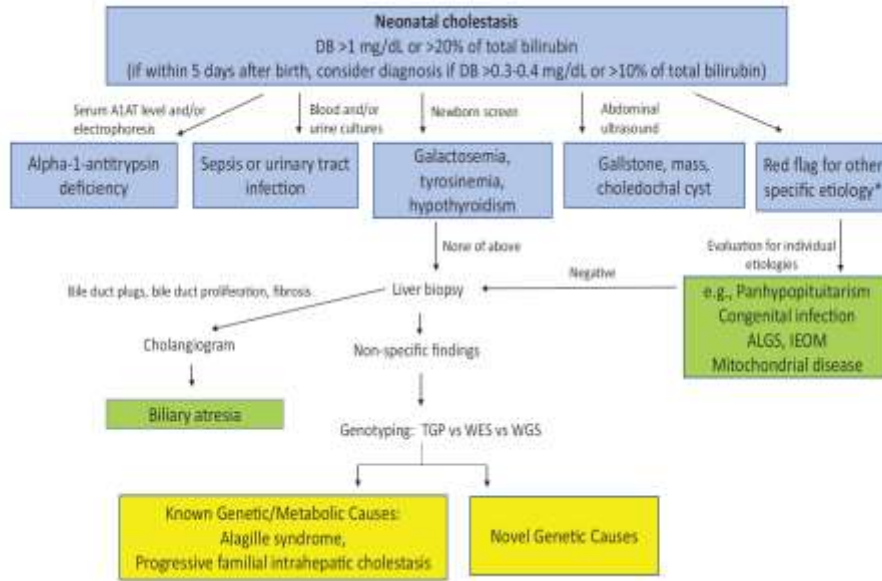


Figure 1: Diagnostic algorithm for the evaluation of neonatal cholestasis

BA, AIAT, and treatable causes of cholestasis (including choledochal cyst, infection, metabolic cause) are quickly excluded through blood tests, imaging, potential liver biopsy and IOC. If there is a “red flag” suggesting a specific diagnosis, the infant should be promptly evaluated for the disease. If a cause is not identified, targeted gene panels (TGP), Whole Exome Sequencing (WES) or Whole Genome Sequencing (WGS) where available can be used to further evaluate for both known genetic/ metabolic causes. IEOM- inborn errors of metabolism, IOC- intraoperative cholangiography, ALGS- Alagille syndrome.

Selected causes of NC

Biliary Atresia: A fibroinflammatory disease with onset in the first months of life that leads to complete obstruction of part of or entire extrahepatic biliary tract, progressive biliary cirrhosis and eventual death.

- occurs in 1 in 6000-18000 live births; sex incidence F > M.

- a leading cause of NC, and the most common cause of end-stage liver disease in children.

- aetiology remains elusive.

Two forms of classification:

a. Clinical: Embryonic /foetal (10-35%), Perinatal (65-90%).

b. Anatomic: (Three types) (i) atretic common bile duct (8%) with patent proximal ducts; (ii) atretic common hepatic ducts and gallbladder, and (iii) atretic right and left hepatic ducts (>80%).

-Diagnosis - See Table III

-Management – Surgery (See above)

Progressive Familial Intrahepatic cholestasis (PFIC): Group of unrelated monogenic disorders in which mutations in one of the genes involved in the canalicular hepatobiliary transport results in progressive cholestasis and liver injury. Many types have been reported.

Alagille Syndrome: Autosomal dominant multisystem disorder characterized by paucity of interlobular bile duct. The diagnosis is usually

clinical (see table on Red flags) and laboratory. It is confirmed by sequencing of JAG 1 and NOTCH 2 genes (mutation in human JAGGED 1 gene on chromosome 20p12)

- Clinical features (See table on Red flags).

- Management: Surgical biliary diversion.

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EXCERPTS FROM THE 2024 PAN WEBINAR SERIES

Overview of Acute Kidney Injury in Children

Odetunde OI

Nephrology Unit, Department of Paediatrics, University of Nigeria Teaching Hospital, Enugu

General Considerations in Acute Kidney Injury (AKI)

Acute Kidney Injury (AKI) is a clinical syndrome manifested by (i) rapid or abrupt decline in kidney function

(ii) subsequent dysregulation of the body electrolytes and volume, and (iii) abnormal retention of nitrogenous wastes.

The widely accepted KDIGO definition of AKI is based on the change of serum creatinine and urine output, as follows:

- Rise in serum creatinine ≥ 0.3 mg/dL within 48 hours
- Rise in serum creatinine ≥ 1.5 times baseline, which is known or presumed to have occurred within the prior seven days
- Urine output < 0.5 mL/kg/hour for six hours

AKI is a wide range of conditions
Not necessarily Acute Kidney failure
Occurring from a wide spectrum of causes.

While many disease processes may cause AKI in children, most share mechanism similarities such as:

- (i) Impaired renal perfusion
- (ii) Direct renal tubular injury

AKI is a broad clinical syndrome encompassing various aetiologies:

- a. Pre-renal azotaemia
- b. Acute tubular necrosis
- c. Acute interstitial nephritis,
- d. Acute glomerular and vasculitic renal disease
- e. Acute post-renal obstructive nephropathy.

GENERAL CONSIDERATION OF AKI		
Aetiology of AKI		
TYPE	Description	Examples
Pre-Renal (Functional)	Renal insufficiency due to inadequate Renal Blood Flow	AGE, Shock, Burns, Haemorrhage, Fulminant hepatitis, CCF, Hepato-renal-syndrome, Reye syndrome etc
Renal (Intrinsic)	Damage to the Kidney	Glomerular Dx: AGN, RPGN Tubular Dx: ATN, ATIN Others: Prolong Prerenal insult, Intravascular Haemolysis (G6PD), Sepsis with MOD, Nephrotoxic drugs, Pf Malaria, Leptospirosis
Post-Renal	Obstruction in the collecting system in the absence of renal parenchymal disease	Bilateral ureteric obstruction... PUJ Bladder-outlet and Urethral obstruction... Calculi, Blood clot and Pus debris.

Both Pre- and Post- Renal AKI conditions can lead to parenchymal injury to kidney (Intrinsic) if prolonged.

Burden

There is limited data about the prevalence of AKI in most African countries.

6.6 to 11.7% of children seen in tertiary institutions with renal disease in Nigeria were reported to have AKI.

Studies of AKI in Nigerian children showed that the main causes were dehydration secondary to

- (i) Gastroenteritis
- (ii) Severe malaria
- (iii) Sepsis
- (iv) Haemoglobinuria
- (v) Drugs: Mini epidemics of Diethylene glycol poisoning.

-More than one of these conditions may coexist in the same patient.

-Epidemiological evidence supports the notion that even mild, reversible AKI has important clinical consequences.

-AKI is increasingly found among critically ill children, following survival from serious illnesses and following major surgeries, especially cardiac surgery.

-It is an important cause of mortality in the hospital setting. Therefore, it is pertinent to identify those at particularly high risk, as there may be no clinical symptoms or signs of early AKI developing.

-There is a greatly increased risk of chronic kidney disease in those who have had an episode of AKI even if there is recovery from acute episode.

-Despite several advances in treatment and in our understanding of the pathogenesis of AKI, many aspects in this field remain subject to controversy, confusion and lack of consensus.

Early Recognition of AKI

-AKI is amenable to prevention, early detection and treatment.

-Clinical practice guidelines in the field thus have the potential to reduce variations, improve outcomes, and reduce costs.

-Early recognition of deteriorating renal functions may aid identification of underlying causes and enable prompt changes in management to avert or minimize AKI.

-Prediction of high-risk factors for AKI can be made, from taking a careful history and meticulous evaluation of renal functions.

-Monitoring is important to detect development and progression of AKI, looking for modifiable factors and underlying causes are also essential.

Early predictor and detector of AKI using the following tools:

- KDIGO Staging
- pRIFLE Staging
- AKIN staging.

-Serum creatinine is a late marker of reduced Glomerular Filtration Rate (GFR), rising only when 25 – 50% of GFR is lost.

-pRIFLE, AKIN and KDIGO Staging are widely used in children and they are dependent on finding a significantly increasing plasma creatinine, or oliguria of $\leq 0.5\text{ml/kg/hour}$.

-Serum creatinine is a late marker of reduced Glomerular Filtration Rate (GFR) rising only when 25 – 50% of GFR is lost.

-Rise of serum creatinine is often delayed and imprecise in AKI, research has focused on identifying biomarkers that accurately predict AKI in the early stages.

Biomarkers of renal injury include:

- Serum Cystatin C
- Neutrophil Gelatinase-Associated Lipocalin (NGAL)
- Kidney Injury Molecule-1 (KIM-1)
- Interleukin-18 (IL-18)
- Biomarkers of renal cell injury may identify additional patients with AKI and may identify the majority of patients at an earlier stage.

Pitfall of Biomarker

Expensive and yet not widely used.

Multiple biomarkers have been studied but none have been clearly identified as reliable predictor of AKI.

Reducing AKI-Related Mortality

The inpatient mortality of AKI varies depending on:

-Severity of staging

-Setting (intensive care or not)

-Patient-related factors

-Typically, be 25–50% or more

- The strategies that prevent AKI or improve the outcome by reducing the morbidity and mortality of AKI can be adopted from approved management guideline of AKI from KDIGO, NICE Guidelines and others.
- This guideline emphasises early intervention and stresses the importance of risk assessment and prevention, early recognition and treatment.
- It is primarily aimed at the non-specialist clinician, who will care for most children with acute kidney injury in a variety of settings

EARLY RECOGNITION OF AKI

KDIGO Staging of AKI

stage	Serum Creatinine	Urine Output
1	1.5-1.9times baseline or $\geq 0.3\text{mg/dl}$ ($\geq 26.5\text{ml/L}$) increase	$< 0.5\text{ml/kg/h}$ for 6-12hour
2	2- 2.9 times baseline	$< 0.5\text{ml/kg/h}$ for $\geq 12\text{h}$
3	3.0 times baseline OR $\text{SCr} \geq 4.0\text{mg/dl}$ ($\geq 353.6\text{umol/L}$) OR initiation of renal replacement therapy or $\text{eGFR} < 35\text{ml/mn per } 1.73\text{ml}$ ($< 18\text{ years}$)	$< 0.3\text{ml/kg/hour}$ for 24h OR Anuria $\geq 12\text{h}$

EARLY RECOGNITION OF AKI

pRIFLE Staging	GFR Criteria	Urine Output Criteria
Risk	Increase $\text{SCr} \times 1.5$ or GFR decrease $> 25\%$	$\text{UO} < 0.5\text{ml/Kg/hr} \times 6\text{hr}$
Injury	Increase $\text{SCr} \times 2$ or GFR decrease $> 50\%$	$\text{UO} < 0.5\text{ml/Kg/hr} \times 12\text{hrs}$
Failure	Increase $\text{SCr} \times 3$ or GFR decrease $> 75\%$ OR $\text{SCr} > 4\text{mg/dl}$	$\text{UO} < 0.3\text{ml/Kg/hr} \times 24\text{hrs}$ or Anuria $\times 12\text{ hr}$
Loss	Complete loss of kidney function $> 4\text{ week}$	
ESKD	End Stage Kidney Disease (function loss for $> 3\text{month}$)	

The recommendations aim to address known and unacceptable variations in recognition, assessment, initial treatment and referral for renal replacement therapy.

- Monitoring of the renal functions of children with high risk.
- Early awareness and avoidance of AKI.
- Identification of high-risk patients.
- Monitoring of renal function, risk stratification and the use of biomarkers.
- Early intervention: removal or modification of contributing factors or causes.

- Early discussion with nephrology specialists when they do not primarily manage the patient.
- Tailoring of management to AKI stage.
- Evaluation of children with AKI promptly to determine the cause, with special attention to reversible causes.
- Monitoring of children with AKI with measurements of serum creatinine (SCr) and urine output to stage the severity of the condition, according to KDIGO or pRIFLE or AKIN.

It is important to:

-Manage children with AKI according to the stage and cause.

- Evaluate affected children three months after AKI for resolution, new onset, or worsening of pre-existing chronic kidney disease (CKD).
- Send a child to a nephrology centre for appropriate evaluation and follow-up if the child has CKD or risk for CKD.

Prevention

-In view of the frequency and high mortality rate associated with AKI, prevention or amelioration of cases of AKI will prevent morbidity and mortality and substantially reduce complications and their associated costs of management.

-This is the best form of management

-The components of prevention include the following:

1. **General health promotion.**
 - a. Education – avoid nephrotoxic drugs (special mention – preterm infants), traditional herbal concoctions, aminoglycosides, NSAIDs, Angiotensin Converting Enzyme Inhibitors/ARBs.
 - b. World Kidney Day activities to create awareness and provide opportunities for screening.
 - c. Liberal water intake.
2. **Specific health protection**
 - a. Screening – urinalysis, blood pressure
 - b. School health program
 - c. 3Ms (Monitor, Maintain, Minimize) in high-risk groups
3. **Early diagnosis and prompt intervention**
 - a. Clinical – History, Peripheral pulses, Blood Pressure
 - b. Biochemical - Serum Urea/Electrolytes/Creatinine, Urine chemistry
 - c. Radiological - Imaging (Ultrasonographic scanning)

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Management of Acute Kidney Injury

Obiagwu PN

Department of Paediatrics, Bayero University Kano/ Aminu Kano Teaching Hospital, Kano

Management of AKI

This depends on the identified cause of the AKI.

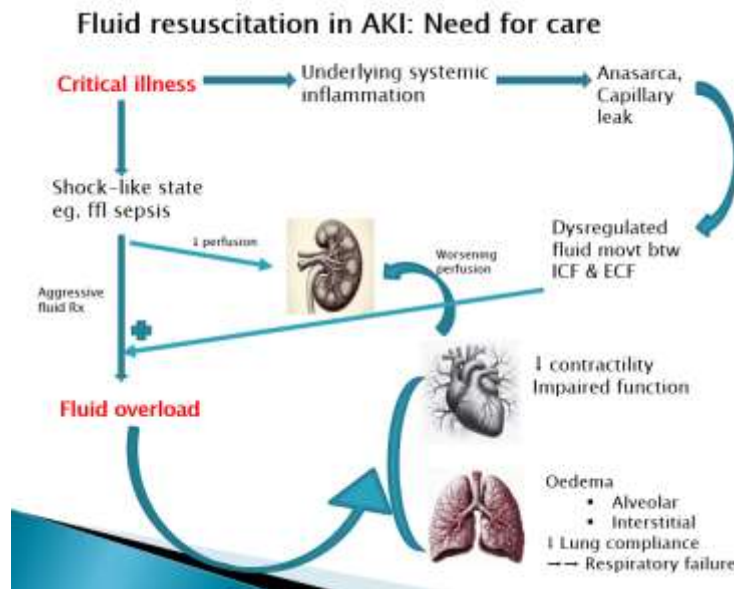
- Obstructive causes require surgical intervention.
- Ranges from conservative medical management to kidney replacement therapies.
- Depends on the:
 1. severity of kidney disease.
 2. degree of kidney function recovery.

Management Principles

- Maintain kidney perfusion and fluid balance.
- Correct electrolytes/acid-base derangements.
- Control blood pressure.
- Treat anaemia if present.
- Provide adequate nutrition.
- Adjust medications for the degree of kidney impairment.
- Initiate kidney replacement therapy (dialysis) when indicated.

Kidney perfusion and fluid balance

- For oliguria or AKI with haemodynamic instability.
- Fluid challenge with normal saline at the rate of 10-20mls/kg rapidly (contraindicated in volume overload).
- Repeat fluid boluses (not more than thrice) may be needed if the child remains haemodynamically unstable – a situation common in sepsis.
- Give Frusemide 1-2mg/kg after restoring intravascular volume if the child does not make urine.
- If no diuresis occurs, the child should be managed as a case of established kidney failure.
- Reduce fluid intake to 300-400mls/m²/day D5W plus previous day's fluid output.
- Some studies have shown that, in critical illness:
 - A more conservative fluid regimen guarantees more ventilator/ICU-free days.
 - Fluid overload or increased fluid administration is independently associated with mortality in AKI.



Electrolytes, Acid-Base Balance

- Sometimes, the derangement encountered depends on the aetiology of the AKI.
- Some of the electrolyte derangements include:

- Hyponatraemia
- Metabolic acidosis
- Hyperkalaemia

- Hyperphosphataemia (with hypocalcaemia)
- Hyponatraemia

-The pre-AKI status of the child, if known, is important. For example, salt-wasting disorders need continuous sodium supplementation.

-Determine fluid status – hypovolaemia, euvolaemia or hypervolaemia.

-If hyponatraemia is due to

- salt depletion – replace with appropriate fluid
- water retention – fluid restriction or water removal.

Metabolic acidosis

-Normally the kidneys excrete generated acids.

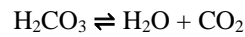
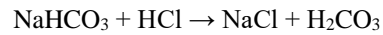
-Treatment of severe metabolic acidosis include:

- Oral or IV sodium bicarbonate
- Sodium citrate
- Dialysis therapy

Notes

-Check serum ionized Ca: Treatment of acidosis can decrease ionized Ca and precipitate seizures/tetany.

-Intact respiration is necessary to excrete generated CO₂.



Hyperkalaemia

-Serum potassium $\geq 5.5\text{mEq/L}$.

-Can be life-threatening.

-Some clinical symptoms include

- Fatigue
- Palpitations or syncope
- Muscle weakness and/or tenderness
- Paraesthesia
- Flaccid paralysis
- Depressed deep tendon reflexes

Hyperkalaemia – ECG abnormalities

K (meq/L)	ECG picture
>5.5	Tall, tented T waves
>6.5	Prolonged PR interval with flattening of the P wave
	ST segment depression
>7.5	Widening of the QRS complex
	Amplified R wave
>8	Intraventricular/Fascicular/Bundle branch blocks
	Arrhythmias (Ventricular Fibrillation/Asystole)

Urgency of hyperkalaemia management depends on:

- Rate of rise of potassium.
- Absolute level of serum potassium.
- Presence of clinical symptoms/ECG changes.
- Underlying cause of hyperkalemia.

Note: Absence of ECG does not delay treatment

Non-urgent management

K⁺ = 5.5 to 6.4mEq/L, no clinical symptoms or ECG abnormality

Enhance K⁺ excretion using ion-exchange resins and/or diuretics

More urgent/aggressive management

K⁺ $\geq 5.5\text{mEq/L}$ with presence of clinical symptoms and/or any ECG abnormality

K⁺ $\geq 6.5\text{mEq/L}$

Practical management of Hyperkalaemia

Step 1

Stop all exogenous sources of K⁺

IV, oral, transfusions, total parenteral nutrition

Step 2

Apply ECG leads for continuous **ECG** monitoring

Step 3

Stabilization of the myocardial cell membrane

Use calcium gluconate or calcium chloride

Step 4

Enhance K⁺ uptake by the cells

Use insulin/glucose, β-agonists, sodium bicarbonate

-

Step 5

Enhance renal excretion of K⁺

Diuretics, ion-exchange resins

Step 6

Eliminate K⁺ from the body

Dialysis – Peritoneal dialysis or Haemodialysis

Monitoring

The following parameters should be monitored:

- Serum potassium 2-hourly.
- Blood glucose (if insulin is used).
- Cardiac monitoring – continuously.

Stepwise Prescription

Item	Dose	Effect	Note
Calcium gluconate	1ml/kg over 5 – 10mins	Counteracts cardiac effects of K	Ensure cardiac monitoring
50% glucose + Insulin	1ml/kg + 0.1u/kg	Drives K into cells	If hyperglycaemic, insulin only, with care
Salbutamol nebulized or IV	5 – 10mg or 4µg/kg	Drives K into cells	3 – 4 times bronchodilation dose
Sodium bicarbonate	1mEq/kg over 10 mins	Drives K into cells	Give if acidotic Infusion preferred over bolus
Furosemide	1mg/kg 12hrly	Enhances K elimination	Used in preserved kidney function
Ion-exchange resin • Resonium A • Kayexalate	0.5g/kg 1g/kg	Exchanges Na for K Takes about 2 hours	
Dialysis		Eliminates K from the body	

Indications for Acute Dialysis

A – Acid-base problems (severe metabolic acidosis)

E – Electrolyte problems (severe hyperkalaemia)

I – Intoxications (poisoning from salicylates, ethylene glycol)

O – Overload (severe fluid overload)

U – Uraemic symptoms (pericarditis, encephalopathy, bleeding diathesis)

Blood Pressure Control

-Raised BP is usually due to volume overload or changes in vascular tone.

-If the child cannot take orally or if severe HTN exists, IV medications are preferable.

-Useful medications include:

- Sodium nitroprusside
- Labetalol

- Nicardipine
- Hydralazine
- Nifedipine (sublingual) etc

Anaemia management

-Children with AKI and anaemia do not usually need blood transfusions except if the haemoglobin concentration falls below 7g/dL.

-Exceptions to this rule include the following:

- Ongoing significant blood loss.
- Symptomatic anaemia with haemodynamic instability.
- Certain underlying clinical conditions such as cardiac conditions – where transfusion threshold is higher at haemoglobin concentration of 8-9g/dL.

- In a fluid-overloaded child who requires HD and blood transfusion, intra-dialysis transfusion is preferred.
- Erythropoietin - not found to have any impact.

Nutrition management

AKI is a catabolic state and malnutrition is common.

This condition is to be co-manage with a renal nutritionist/dietitian using:

- (i) Protein and energy-dense feeds, preferably oral.
- (ii) Breastmilk/low phosphorus formula in infants.
- (iii) Proteins of high biologic value in older children: 0.5 – 2g/kg/day
- (iv) Increased intake of calories
 - carbohydrate >70%
 - fat <20% (so child would not be catabolic)
- (v) Decreased intake of Na⁺, K⁺

Medication adjustments

-Doses of certain medications may need to be adjusted based on the degree of kidney function derangement.

-This requires checking prescribed medications which are eliminated via the kidneys, and adjusting doses appropriately.

Peritoneal Dialysis

- Performed at the bedside/on the ward.
- Prescription is individualized.
- Improvised PD if commercial consumables are not available.
- Quicker initiation of therapy.
- May be less efficient than HD in certain situations eg severe hyperkalaemia.
- Better tolerated than HD.

Haemodialysis

- Patient is taken to the dialysis unit.
- Prescription is individualized.
- There may be logistic challenges.
- Procuring appropriately-sized consumables (lines, dialyzers, catheters) for children
- Availability of space on appropriate machine
- Need for good support by the adult nephrologists/nephrology nurses in the center

Special situation: AKI in the Neonate

-Neonates are a high-risk group.

-Some challenges in AKI identification in the neonate.

-Kidney functions are worse with lower gestational age and birth weight – due to fewer nephrons and lesser maturity of the nephrons.

-sCr taken in first few days reflects maternal values.

-sCr is a delayed marker of kidney function and other biomarkers are not yet in routine use.

-Urine output measurement in the neonate is tasking.

Neonatal-modified KDIGO definitions

sCr ≥ 26.5µmol/L (0.3mg/dL) within 48hour or urine output (UO) < 0.5ml/kg/hour for 6-12hours – Stage 1.

sCr ≥ 220µmol/L (2.5mg/dL) - Stage 3.

40 – 70% higher prevalence rates of AKI occur in:

- Premature/Low birth weight
- Cardiac conditions (congenital heart disease/cardiac surgery)
- Perinatal asphyxia with HIE
- Necrotizing enterocolitis (NEC)
- Receiving nephrotoxic medications

-Theophylline – reduces the risk of AKI in severe asphyxia.

-Caffeine – reduces the risk of AKI in preterm babies and in NEC

Follow-Up in AKI

-10% of AKI survivors continue to be at a high risk for kidney dysfunction for three to five years.

-The figure is much worse with:

- Stages 2 and 3 AKI
- Background CAKUT and/or CKD
- Neonates
- AKI associated with multi-organ dysfunction

Evaluate the child 3, 6, 12, 24 months after AKI.

Precautionary measures

DO NOT.....

-Assume that serum creatinine in the ‘normal range’ on your hospital laboratory form is normal for the child.

-Think that urine output is normal because “the caregiver says so”. Catheterize the patient and actually measure the urine to confirm.

- Keep giving fluid after three boluses because you are “not quite comfortable” with the perfusion. Have a re-think. Reassess.
- Wait for the child to have defined stage 3 AKI before considering Kidney Replacement Therapy (KRT). Earlier KRT may save the child.
- Assume that a ‘three-day history of illness’ means the child cannot have CKD. Evaluate fully.
- Give ‘half of adult dose’ of medications to small children. Check the BNF, EMDEX, Google or just call a paediatrician colleague to confirm.
- Shy away from discussing challenging cases with paediatrician colleagues (nephrology residents, nephrologists).

When to seek a nephrologist review

- Presence of dialysis indications.
- Severe AKI (Stages 2 and 3).
- Inadequate response to management.
- Kidney transplant, known CKD or CAKUT
- Diagnosis requiring specialist intervention (vasculitis, tubulointerstitial nephritis).
- Recovered AKI but with hypertension, impaired kidney function or proteinuria.
- Neonatal AKI

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Questions on AKI Management

1. A 6-year-old child presents with fever, vomiting, and decreased urine output. On examination, blood pressure is elevated. Laboratory findings show elevated serum creatinine. What is the initial management for this child?
 - a) Intravenous fluids
 - b) Diuretics
 - c) Antibiotics
 - d) Blood transfusion
 - e) Dialysis
2. A 10-year-old boy with AKI has serum potassium level of 6.7mmol/L. Which medication should be administered promptly?
 - a) Furosemide
 - b) Calcium gluconate
 - c) Sodium bicarbonate
 - d) Insulin and glucose
 - e) Albuterol
3. A 4-year-old girl with AKI is malnourished. What nutritional intervention is essential for her management?
 - a) High-protein diet
 - b) Low-sodium diet
 - c) Enteral nutrition
 - d) Parenteral nutrition
 - e) Low-potassium diet
4. A 5-year-old girl with AKI develops severe metabolic acidosis. Which pharmacotherapeutic intervention helps correct acid-base balance?
 - a) Sodium bicarbonate
 - b) Potassium chloride
 - c) Calcium carbonate
 - d) Magnesium sulfate
 - e) Ammonium chloride
5. A 12-year-old girl with AKI has fluid overload with severe anaemia. Which of the following interventions would be most appropriate?
 - a) Blood transfusion after haemodialysis
 - b) Peritoneal dialysis with 10% mannitol
 - c) Continuous renal replacement therapy
 - d) Blood transfusion during haemodialysis
 - e) Blood transfusion before haemodialysis

Key:

Question	Correct Option
1	A
2	B
3	C
4	A
5	D

Care of the Small and Sick Newborn - Bridging the Gaps

Mukhtar-Yola M

President, NISONM

Department of Paediatrics, National Hospital, Abuja.

Who is the small and sick newborn?

- This includes newborns who are small from prematurity, low birth weight, and/or small for their gestational age — and/or are sick.
- These sicknesses could include breathing problems, infections, intrapartum-related complications, pathological jaundice, metabolic issues, feeding problems, temperature instability, haemodynamic instability and others.
- Approximately 80% of the 2.4 million annual global newborn deaths are LBW; two - thirds of the deaths are preterm babies.
 - They are at high risk of dying or becoming disabled; estimated 1 million survivors end up with a long-term disability.

Magnitude of the problem: Preterm birth

- Each year, 11% of the world's babies are "Born too Soon" resulting in about 15 million preterm babies.
- WHO in 2015 reported prematurity as the leading cause of Under-5 deaths globally and 60% of the world's preterm births occur in Asia and sub-Saharan Africa – low resources for care and lower survival.
- Nigeria ranks third among the countries with the highest number of preterm births globally - 75% of these deaths could be prevented if current interventions were used.
- Neonatal Mortality rate is currently 39/1000 in Nigeria.

Global burden of LBW

- Every year 20 million (~15% of all births) infants are born with LBW and >95% of these are in LMICs.
- Account for 70-80% of all neonatal deaths.
- Reducing mortality in LBW will be important in attaining the SDG

Outcomes in HIC vs MIC Vs LICs

- Ninety-eight per cent of neonatal deaths occur in LMIC countries, with 75% occurring in Southern Asia and SSA.
- Of the 10 countries with the highest NMRs, eight are in Africa.
- In HICs, the NMR is usually low, and most small newborns survive and thrive.
- In MICs, the risk of disability for infants born between 28 and 32 weeks of gestation is nearly double that of HICs, due to deficiencies in the quality of care.
- In LICs, disability is not so common since the smallest and sickest newborns, usually die due to lack of access to essential care or more advanced care when needed.

Breathing Problems

Breathing problems are the most common clinical presentations in sick and small neonates.

Causes are quite diverse: may be respiratory or non-respiratory in origin.

- Respiratory Distress Syndrome (RDS)
- RDS occurs primarily in preterm babies; incidence is inversely related to gestational age and birth weight.
- There is reduced risk with antenatal steroid use (Dexamethasone or Betamethasone).

Managing Respiratory distress

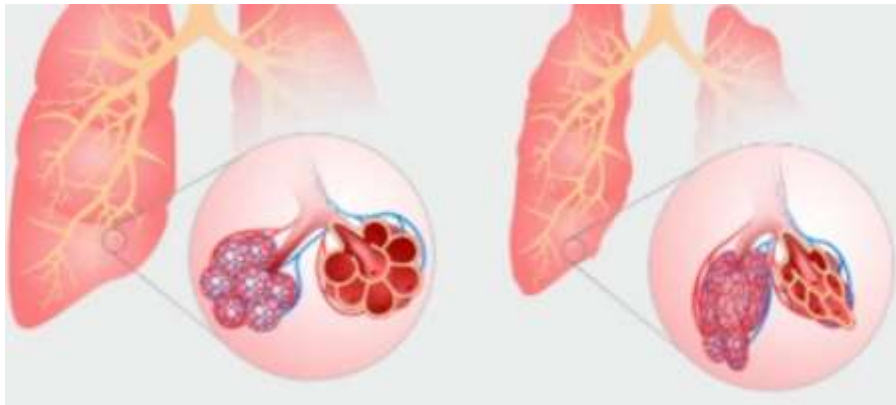
- i. Accurate assessment of respiratory distress using the Downes, Anderson Silverman's, or WHO scoring systems
- ii. Investigations including the SPO₂, blood gases, radiology, and sepsis.
- iii. Oxygen therapy.
- iv. Non-invasive ventilation.
- v. Continuous Positive Airway Pressure (CPAP).
 - Bubble CPAP.
 - Variable flow Nasal CPAP.
 - CPAP mode on a ventilator.

- vi. Invasive Ventilation using a mechanical ventilator.
- vii. Use of surfactant.
- viii. Caffeine citrate therapy.
- ix. Addressing underlying causes and complications.
- x. Supportive care.

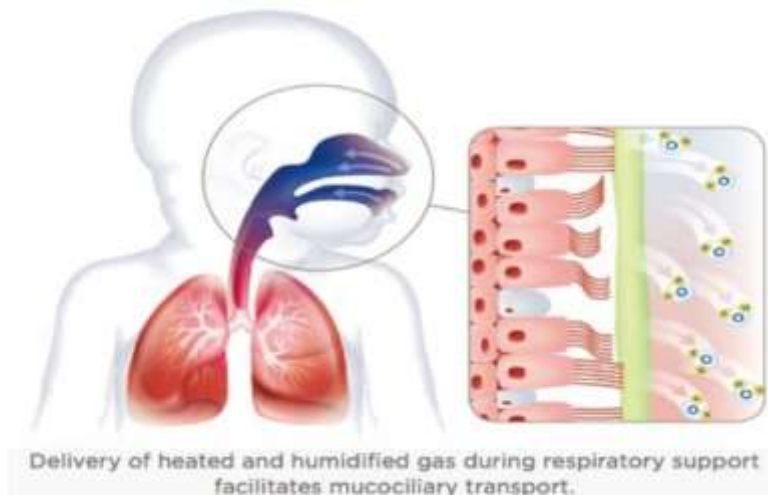
-There is currently, a global shift towards the use of non-invasive respiratory support for preterm babies with RDS, hallmark of which is the application of continuous positive airway pressure (CPAP).
-The benefits of CPAP in the management of respiratory distress syndrome are well documented.
-Goal of CPAP therapy: to maintain normal lung volumes and oxygenation while infants are enabled to breath spontaneously

Continuous Positive Airway Pressure Ventilation (CPAP)

Benefits of CPAP



Promotes airway hydration



Hypothermia

- Thermoneutral environment is vital for the care of small and sick babies
- Hypothermia - skin temperature <36.5°C; Mild, Moderate, Severe.
- Prevalence in hospital-based studies ranged from 32 to 85%

- Risk is increased by 31.3% for every 100 grams below 2000 grams and by 7.4% for every 100 grams below 3000 grams birthweight.
- For every degree drop below 36.5 0 C, there is an 80% increase in mortality risk.
- Low birthweight infants have 11 times the risk of hypothermia compared with normal-weight babies

- Most common in the first 24 hours, delivery room and thereafter.
- In stable babies, emphasis should be on skin-to-skin care and Kangaroo Mother Care (KMC),
 - Unstable babies should be transferred to warming devices for resuscitation.

Kangaroo Mother Care (KMC)

Components:

- Continuous and prolonged skin to skin contact.
- Exclusive breastfeeding.
- Early discharge and adequate follow-up.

What new in KMC?

Key focus is ZERO SEPARATION for a mother and her infant.

Immediate KMC: Evidence shows that simple interventions such as kangaroo mother care immediately after birth, promotes (i) early initiation of breastfeeding within one hour of birth, (ii) use of continuous positive airway pressure (CPAP) from birth and (iii) use of medicines such as caffeine from birth for breathing problems can substantially reduce mortality in preterm and low birthweight babies.

Unless a medical reason exists, healthy mothers and babies should not be separated after birth and during the early days following birth.

Interrupting, delaying, or limiting the time that a mother and her baby spend together may have a harmful effect on their relationship and on breastfeeding success.



New trends in KMC

- KMC has now been extended to babies up to <2500g.
- The duration of KMC is now 8-24 hours.
- The establishment of M-NICUs (mother-NICU) is encouraged.
- For 40 years, the fear of sepsis has been a reason for denying KMC to small and sick newborns.
- The evidence is that KMC dramatically decreases sepsis!

When immediate KMC (iKMC) is compared to controls:

- Death from sepsis: 4.4% vs 6.9 - a reduction of 36%.
- Suspected sepsis: 22.9% vs 27.8% – a reduction of 18%.
- Hypothermia: 5.6% vs 8.3% - a reduction of 35%.

Relative risk of neonatal death subsequent to hypothermia

- A temperature below 35°C has a 10 or 20 times higher chance of death.
- Even between 36°C and 36.4°C, the risk of death doubles.

Challenges in Implementing iKMC

- Policy.
- Financial constraints.
- Perceptions (Other paediatricians, Obstetricians, Parents, Nurses).
- Poor Home Follow-Up (CHEWs)

Summary of Findings

- Immediate KMC for 1.0 and <1.8kg infants significantly reduces the risk of neonatal deaths by 25%.
- Immediate KMC provided to every 27 babies saves a life which translates to 150,000 lives globally every year.
- M – NICU is a paradigm shift in the care of the low-birth-weight infant weight.

The M-NICU:Paradigm shift: Make a difference

M-NICU:

- A facility where sick and small newborns are cared for by their mothers round the clock.

- With all facilities of level II Newborn care & Provision for postnatal care to mothers.

The mother:

- Not a mere visitor, but has a bed inside (resident) the SCBU/NICU
- Is an active caregiver involved in the continuum of neonatal care.
- Buy- in by all stakeholders – management, Obstetricians, Paediatrician/Neonatologist, Nursing.
- National policy change being aligned to permit mother or surrogate in SNCU/NICU everyday

Infections Control

Global estimates of neonatal sepsis:

- Estimates of 1.3 million and 3.9 million annual neonatal sepsis cases and between 400 000 and 700 000 annual deaths occur worldwide
- Among hospital-born infants, hospital-acquired infections account for an estimated 4% to 56% of all deaths in the neonatal period, depending on the study and geographical area investigated
- An estimated 84% of neonatal deaths due to infections could be prevented through measures such as early diagnosis and timely appropriate clinical management
- Lower birth weight and gestational age were associated with increased sepsis incidence.
- 24% of global neonatal deaths are due to severe infections, including sepsis.

Health Care-Associated (HA) Infections

- HA sepsis among all hospital-treated sepsis: 23.6% (95% CI = 17–31.8%)
- Pooled incidence of HA sepsis per 1000 patients = 15.4 (95% CI = 9.2–25.7) in adults, 112.9 cases (95% CI = 64.2–191.1%) in neonates
- 56.6% of all types of HAIs were neonatal HA-sepsis
- The highest neonatal sepsis incidence rates are in LMICs, particularly in the African region.
- HAI rates in Nigeria NICUs range between 4.1% and 25%.

- Neonatal septicaemia occurs at the rate of between 33% and 72.2% - mainly gram-negative organisms.
- Multi-drug resistance in *Klebsiella*. MRSA is particularly deadly.

Common types of HAI in NICU

- Blood stream infections (BSI)
- Central line associated
- Central Venous Catheter (CVC)
- Peripheral inserted central catheter (PICC)
- Umbilical catheter
- Peripheral lines
- Ventilator-associated pneumonia
- Necrotizing enterocolitis
- Surgical site infection (SSI)

Infection Prevention and control skills

- National IPC guidelines are available on the NCDC site, even though mainly tailored to COVID prevention and control.
- Healthcare workers should perform/apply the following skills to prevent transmission of infections:
- Hand hygiene.
- Risk assessment at the point of care.
- Appropriate placement of patients (segregation/isolation/cohort to limit transmission).
- Appropriate use of personal protective equipment, based on risk assessment.
- Respiratory hygiene/cough etiquette.

IPC skills

- Aseptic technique.
- Sharps and injection safety and prevention of transmission of blood-borne pathogens.
- Safe handling and/or disposal of contaminated patient-care items and equipment (waste management).
- Environmental cleaning.
- Linen (safe handling, transporting and processing)
- Decontamination and sterilization of reusable equipment.

Challenges In Neonatal Critical Care

- Funding/resource allocation.
- Health workforce- human resource for newborn health.

- Limited bed spaces: No dedicated NICUs in many centres or inadequate bed space.
- Equipment and their maintenance.
- Non availability of affordable essential medicines such as caffeine citrate and surfactant.
- Fragile nutritional support systems such as breast milk banks.
- Limited data to make informed decisions on strategies of care.
- Personnel Development/capacity building.
- Poor adherence to guidelines/protocol of care.
- Limited water supply/electricity/sanitation.
- Fragile support systems including laboratories and blood banking.
- Family and cultural preferences.

Bridging the Gaps

Capacity building

- Training and re-training of HCW on Helping Babies Breathe, Neonatal Resuscitation Training, Respiratory support workshops, ENCC/CNCC e.g. workshops and seminars, E- learnings; monthly NISONM and PAN webinars, minimal investment with great returns in form of low dose high-frequency training.
- Instituting ENCC in medical and paramedical institutions of training-intensivists, advanced nursing practitioners, physician assistants, biomedical engineers, anaesthetic technicians, respiratory therapists, sonographers, and pharmacists.
- The paucity of well-trained biomedical engineers and anaesthetic technicians has led to a poor maintenance culture of equipment. The CNC training tries to address this challenge.

Health care work force

- The scarcity of healthcare workers and uneven distribution poses a serious challenge. Brain drain and emigration of the workforce.
- In 61 years, the Medical and Dental Council of Nigeria had registered 130,000 doctors. However, in 2023 only 58,000 paid for their annual practising license.

- In 2016; there were 4,618 Nigerian doctors on the GMC register in the UK; this rose to 10,148 in 2022
- About 12,099 Nigerian nurses joined the UK workforce in the six months preceding September 2023 compared to 1,670 same time in 2022.
- Against the backdrop of the WHO's doctor-patient ratio (1:600), Nigeria has a 1:10,000 ratio, and 1:1,160 for nurses.

Bridging health worker shortage

- Strengthening governance framework
- Improved working conditions and welfare of HCW
- Re-balancing healthcare tasks- Task shifting
- Provide a safe working environment
- Developing new care models
- Developing frameworks to train and retain HCW
- Domestic training programs for neonatology and intensive care.
- Creating a sustainable workforce: expand the supply of neonatologists and neonatal nurses; utilize non-intensivist providers in NICUs (abundant and have fewer competing clinical responsibilities compared with specialty-trained intensivists).

Equipment and consumables

- Critical care equipment are scarce in LMICs and when available, are challenging to manage.
- Health research should be directed towards low -cost technology rather than expensive high-tech medical equipment, which requires extensive human, technical and financial resources to maintain.
- Production of needed equipment in LMIC will greatly cut costs of importation. Maintenance should be part of any contract on equipment purchase.

Local adaptations

Local adaptations/ fabrication of equipment should be encouraged as done in India, Nepal and Haiti.

- Improved BCPAP local adaptations
- Sanitizers – pharmacies locally producing alcohol rubs instead of imports

- Parenteral nutrition fluid production locally
- LISA or MIST therapy (Surfactant Replacement Therapy) using French tubes which are readily available, instead of ET tubes for intubation.

Effective data management

- Poor data management in most African records makes projections and planning difficult.
- Lack of data hinders both local and global appreciation of health issues
- Most records are paper based.
- EMR improves the delivery of patient care, complete documentation of a patient's history, reduction in medication errors.
- Important to use simple software that will generate required data sets.

Health Care Financing

- Need for increased budgetary allocation for health.
- Reduce out-of-pocket payments by strengthening insurance systems at government and private and community levels. Since 2014, Only 3% of Nigerians have been captured on the NHIS (NDHS 2018)
- Nigeria, health care budget increased from 3.95% in 2018 (to 4.1% in 2019 and 4.47 % in 2024 falling short of the sector's huge requirements.
- In the 2024 Federal Health Budget, the total sum allocated out of the overall expenditure of ₦27,503,404,073,861 is ₦1,228,100,390,765 inclusive of the ₦ 125,737,146,031 provided for the Basic Health Care Provision Fund (BHCPF).

Preventive care

-Preventive care- improving social determinants of health.

-These indices are still low in Nigeria:

- access to water - 66% have access to an improved source of drinking water;
- sanitation - 56% of Nigerian households use an improved sanitation facility
- electricity - 59% of households have electricity

- education - overall, 36% of females and 27% of males in Nigeria have no education. (NDHS 2018).

Progress in Neonatal Medicine in Nigeria- 16 years of NISONM

- Advocated for a newborn desk officer at the Federal Ministry of Health.
- Development of several Neonatal National Guidelines and training manuals in collaboration with the Federal Ministry of Health and other partners.
- Collaborations/partnerships with international and multinationals on newborn health issues and equipment sourcing.
- Capacity Building on HBB/NRT supported by PAN over 16 years along with other workshops across the country
- More NICUs opened and equipped through collaborations with the government, UNICEF, NEST 360, MCGL/JPIEGO.
- Inclusion of newborn essential medicines into the Essential Medical list.
- Many more centres can now offer respiratory support for newborns.
- Many centres have infection prevention mechanisms using simple protocols, consumables and equipment.
- Collaborations with the WACP and NPMCN to establish the neonatology subspeciality fellowship.
- The advent of the Neonatal Nursing program. viz six pilot sites.
- The use of EMR in several sites to generate data
- Collaborations around capacity building and research with several International organizations and the African neonatal network.

Conclusion

While we strive to match global best practices, we must continue to, find/ adapt local solutions and develop a maintenance culture. Prevention, early diagnosis and prompt treatment are key to success.

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Questions on Care of the Small and Sick Infant

1. Which of the following is not a new learning in KMC?
 - a. Concept of M-NICU
 - b. Promotion of IKMC
 - c. KMC lasts 4-16 hours daily
 - d. Family centered care
2. Which of the statements below describes the most effective strategy in Infection prevention and control?
 - a. Effective hand hygiene
 - b. Risk assessment at the point of care
 - c. Appropriate placement of patients
 - d. Use of personal protective equipment
3. Which of the following statement is true about CPAP?
 - a. It is a form of invasive ventilation
 - b. It maintains normal lung volumes and oxygenation
 - c. It cannot be used in KMC position
 - d. It cannot be used in term infants
4. Which of the following is a valid statement regarding hypothermia?
 - a. For every degree drop below 36.5⁰ C, there is an 80% increase in mortality risk.
 - b. Low birthweight infants have 11 times the risk of hypothermia compared with normal-weight babies
 - c. Most common after the first 24 hours in small and sick newborns
 - d. In stable babies, emphasis should be on skin-to-skin care
5. Which of the following is not helpful as a ventilatory support for low birth weight babies?
 - a. Bubble CPAP
 - b. Caffeine citrate
 - c. Surfactant
 - d. Betamethasone

Keys:

Question	Correct option
1	C
2	A
3	B
4	C
5	D

CLINICAL QUIZ

A clinical scenario and the corresponding clinical image are provided below. Please study the image and answer the questions.

The image displayed below belongs to Joy, a six-month old female infant who was admitted with a history of failure to gain weight of four months duration, recurrent cough and fever of two months duration. Her father was known to have had a long-standing cough with weight loss and was receiving treatment at the DOTS clinic nearby. Joy's weight-for-length Z-Score plotted on -3.5SD.



Source: The Union Diagnostic Atlas for Tuberculosis in Children

1. What is the most likely diagnosis?
 2. What other major presenting complaints could Joy have had?
 3. What physical examination findings in Joy will be typical of the conditions?
 4. What obvious complication of the condition did Joy have at presentation?
 5. What complications may Joy subsequently develop?
 6. What are the risk factors for this condition?
 7. What should constitute management including drugs and in what specified duration that will effectively treat Joy's primary condition?
 8. What is also crucial in Joy's management that will prevent a recurrence in Joy and her siblings?
- The answers are provided on the next page.

Hassan-Hanga F.

**Chief Consultant Paediatrician, Kano State Paediatric TB Focal Point, Paediatric HIV Coordinator.
Paediatrics Department, Aminu Kano Teaching Hospital/Bayero University, Kano, Kano State.**

Questions	Answers
1. What is the most likely diagnosis?	Miliary Tuberculosis
2. What other major presenting complaints could Joy have had?	<ul style="list-style-type: none"> • Laboured breathing • Poor feeding • Seizures • Altered consciousness • Stiff neck • Behavioural changes • Confusion
3. What physical examination findings in Joy will be typical of the conditions?	<ul style="list-style-type: none"> • Generalized lymphadenopathy • Choroid tubercles • Crepitations/Wheezing • Hepatosplenomegaly
4. What obvious complication of the condition did Joy have at presentation?	<ul style="list-style-type: none"> • Severe Acute Malnutrition
5. What complications may Joy subsequently develop?	<ul style="list-style-type: none"> • Respiratory distress, hypoxia, pneumothorax or pneumomediastinum from Alveolar-air block syndrome • Tuberculous meningitis that can extend to the brainstem leading to deficits of cranial nerves III, VI, and VII. • Abdominal tenderness of tuberculous peritonitis. • Cutaneous papulo-necrotic tuberculids, nodules, or purpuric lesions. • Choroid tubercles.
6. What are the risk factors for this condition?	<ul style="list-style-type: none"> • Infants and young children under five years of age • HIV, malnutrition, and immunosuppression from other causes like Type 2 Diabetes mellitus, End-Stage Kidney Disease, Malignancy • Overcrowding • Close contact with an adolescent or adult with active TB • Lack of BCG immunisation
7. What should constitute management including drugs and in what specified duration that will effectively treat Joy's primary condition?	<ul style="list-style-type: none"> • Antitubercular therapy (ATT): Isoniazid, Rifampicin, Ethambutol, and Pyrazinamide for the intensive phase of two months, followed by a continuation phase of four months of rifampicin and isoniazid. • Joy is not eligible for the four-month regimen recently recommended for drug sensitive tuberculosis by WHO since miliary TB is a severe presentation. • Supportive care: Nutritional support, management of complications. • Corticosteroids: for severe symptoms or CNS involvement.
8. What is also crucial in Joy's management that will prevent a recurrence in Joy and her siblings?	<ul style="list-style-type: none"> • Source identification and active TB treatment. • Contact tracing and active/latent TB treatment according to identified TB status.