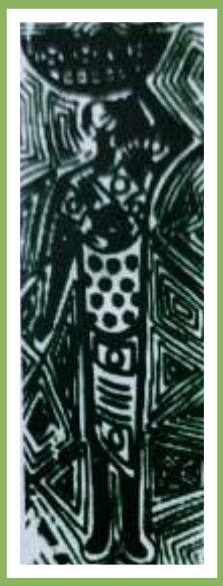
NIGERIAN JOURNAL OF PAEDIATRICS

OFFICIAL JOURNAL OF THE PAEDIATRIC ASSOCIATION OF NIGERIA



VOLUME 51
NUMBER 3
JULY - SEPTEMBER 2024

https://www.njpaediatrics.com
PRINT: ISSN 0302-4660
ONLINE: ISSN 2814-2985

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Nigerian Journal of Paediatrics

Volume 51 Number 3
July-September 2024

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CASE REPORT

EDUCATIONAL SERIES

EDUCATIONAL SERIES

Nigerian Journal of Paediatrics 2024; Volume 51(3): ES024-ES055.

https://dx.doi.org/10.4314/njp.v51i3.09.

SYNOPSIS: VITAMIN D-RESISTANT RICKETS

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Case Presentation

A boy aged 2-years 8months, presented with progressively worsening, painful abnormal gait and swelling of the wrists, knees and ankles for about a year. He walked at 10 months of age but was noticed to have an abnormal gait. The parents were reassured by neighbours that it was normal and would be self-limiting.

He was adopted a few days after birth, and he is the only child of his parents, who are in their forties. He was formula-fed on demand for six months, and thereafter, home-made maize gruel and soyabean powder was added. He was fed about five times a day. By age one year, he was already on regular home staple foods. He lived with his parents in a three-bedroom apartment on the first floor of a two-storey-building. Both parents were school teachers, and he was usually taken to school with them, and also played with other children. There was no chronic drug history, except for multivitamins from time to time. He has had no cause for hospital visits except for immunization.

Examination findings: A cheerful toddler who weighed 12kg (15th centile for age) with standing height of 85cm (<3rd centile for age), occipitofrontal circumference of 51cm (between 75th and 90th centiles for age) and mid arm circumference of 15.3cm. There was no pallor, jaundice or oedema. The liver, spleen and kidneys were not palpable. He walked with a waddling gait and his wrists, knees and ankles were swollen as shown in Figure 1.

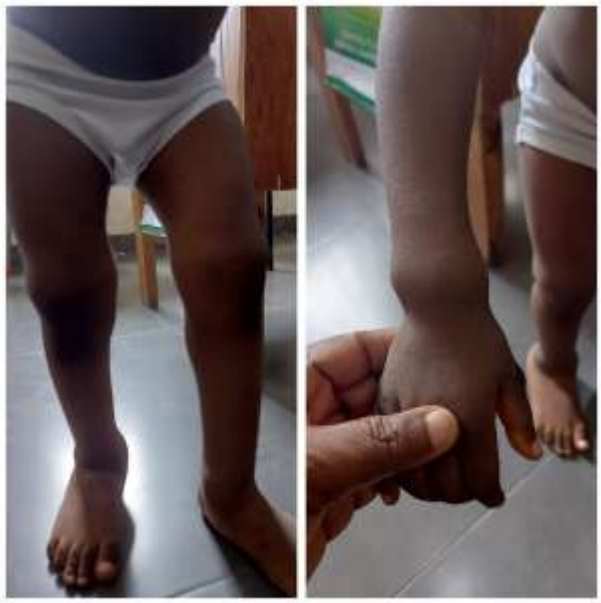

Figure 1: Swelling of the wrist, knee and ankle joints

At the initial visit, he was commenced on oral Vitamin D3 2000IU daily while the following investigations were ordered: X-rays of wrists and lower limbs (Figure 2), serum alkaline phosphatase, serum calcium and inorganic phosphate, serum vitamin D level and Haemoglobin genotype. The child was reviewed on out-patient basis on monthly intervals for two more months, and each time, he had a recast of the oral Vitamin D3 in the same dose. A repeat of the x-rays and biochemistry tests were carried out by the third visit. At this visit, oral calcium carbonate 300mg tablet daily was prescribed. The results of investigations are as shown in Table I.

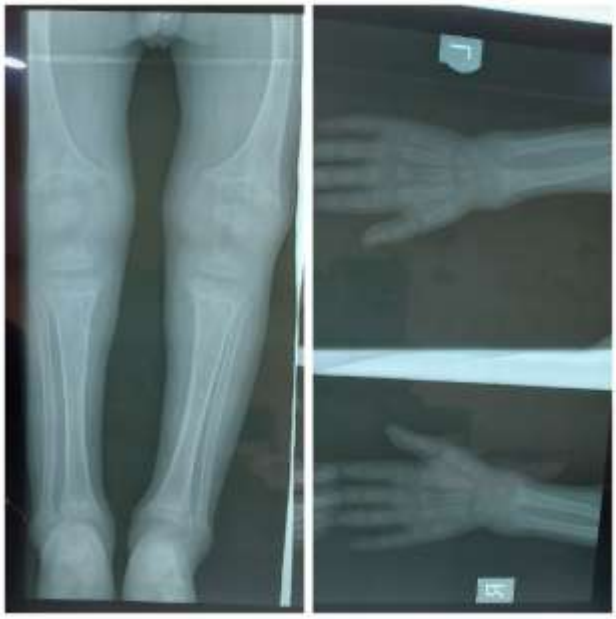

Figure 2: X-rays showing bowed femur; cupping, fraying and widening of the metaphyses, soft tissue swellings of the wrists, knees and ankles and rarefaction of the bones.

Table I: Results of laboratory investigations

Investigation	Initial Result	Repeat Result after 72 days of oral Vit. D3	Laboratory Reference Value
Haemoglobin genotype	AA	-	-
Serum alkaline phosphatase	3319 U/L	2811 U/L	<281 U/L
Serum Calcium	2.19 mmol/L	2.06 mmol/L	2.24 – 2.74 mmo/L
Serum Inorganic phosphate	0.56 mmol/L	0.80 mmol/L	0.81 – 1.45 mmol/L
Serum Vitamin D	33.3ng/ml	Not done (cost consideration)	<12ng/ml (deficient) 12 – 20ng/ml (insufficient) >20ng/ml (sufficient)
Repeat X-rays showed no interval change			

Overview of Rickets

Rickets is a condition in children characterized by impaired bone mineralization, leading to soft and weak bones. It typically results from a deficiency in vitamin D, calcium, or phosphate and can lead to bone deformities and growth disturbances. Long bones are mostly affected.

Rickets may be classified into two broad groups:

1) **Calcipaenic rickets:** This follows a reduced quantity of calcium which occurs in:

a) Vitamin D deficiency/resistance
b) Dietary deficiency - inadequate vitamin D from dietary sources
c) Malabsorption disorders- affect absorption from the gut
d) Limited exposure to sunlight
e) Liver disease – may result in defective 25-hydroxylation which normally occurs in the liver
f) Drug-induced Rickets: Certain medications can interfere with vitamin D metabolism (25-hydroxylation) or bone mineralization, leading to rickets. Examples include anticonvulsants like phenytoin and phenobarbitone, which enhance the degradation of vitamin D, or

bisphosphonates, which can affect bone mineralization.

g) Vitamin D-Dependent Rickets Type 1 (VDDR1): A genetic disorder caused by mutations in the gene coding for the enzyme 25-(OH) vitamin D 1α-hydroxylase (CYP27B1), which is necessary for converting 25-(OH) vitamin D into its active form (1,25-$(OH)_2$ vitamin D.

h) Vitamin D-Dependent Rickets Type 2 (VDDR2): A disorder caused by mutations in the vitamin D receptor (VDR) gene, leading to resistance to the effects of active vitamin D (end organ resistance).

i) Deficiency of calcium - Occurs when there is insufficient calcium intake, often due to dietary inadequacies or malabsorption syndromes.

j) Renal osteodystrophy of chronic kidney disease (renal rickets) – there is reduced 1,25-hydroxylation in the kidneys.

2) **Phosphopaenic rickets** – Phosphate deficiency rickets: Less common and usually results from specific dietary deficiencies or conditions that cause inorganic phosphate wasting.

a) Phosphate loss as a result of genetic mutations - In these conditions, even with normal vitamin D levels, the renal handling of phosphate is impaired. This leads to low serum phosphate levels, which is a critical component of bone mineralization. This results in rickets or osteomalacia (softening of the bones). Examples include:

b) X-linked hypophosphataemic rickets (XLHR): This is the most common form and is caused by mutations in the PHEX gene, which leads to excessive levels of fibroblast growth factor 23 (FGF23). FGF23 decreases renal phosphate reabsorption and reduces the activation of vitamin D.

c) Autosomal dominant hypophosphataemic rickets (ADHR): Caused by mutations in the FGF23 gene itself, leading to its resistance to degradation and, subsequently, persistent hypophosphatemia.

d) Autosomal recessive hypophosphataemic rickets (ARHR): Caused by mutations in the DMP1 or ENPP1 genes, leading to similar mechanisms of hypophosphatemia due to altered FGF23 regulation.

e) Hereditary hypophosphataemic rickets with hypercalciuria (HHRH).

f) Fanconi Syndrome – Here a malfunction of the proximal tubules results in massive urinary phosphate loss causing hypophosphataemic rickets.

g) Dietary phosphate deficiency.

h) Malabsorption of phosphate.

Table II: Salient features of different types of rickets [culled from R. Chanchlani *et al.*]

Type of Rickets	Calcium	Phosphate	Alkaline phosphatase	Parathyroid hormone	25 (OH) Vitamin D	1,25 $(OH)_2$ Vitamin D
Calcipaenic						
Vit D deficiency	↓ or N	↓ or N	↑ or ↑↑	↑	↓	Variable
VDDR type 1	↓	↓ or N	↑↑	↑	N	↓
VDDR type 2	↓	↓ or N	↑↑	↑	N	N or ↓
Phosphopaenic						
Nutritional PO_4 def	↑ or N	↓	↑ or ↑↑	↓ or N	N	↑
XLHR	N	↓	↑	N or slight ↑	N	N or ↓
ADHR	N	↓	↑	N	N	↓
ARHR	N	↓	↑	N	N	↓
HHR with hypercalciuria	N	↓	↑	N or ↓	N	↑

N - Normal serum levels; ↓ - Decreased serum levels; ↑ - Increased serum levels

Comparing the results obtained from the patient (Table I) to the features in Table II, it appears the index case had calcipaenic rickets of VDDR Type 1 or 2. The serum level of 1, 25-hydroxy Vit D was not assayed. This would have made the distinction between the two types.

Vitamin D-Resistant rickets

Vitamin D-dependent rickets (VDDR) is a rare form of rickets characterized by defects in the metabolism of vitamin D, which affects bone development. There are two main types: VDDR Type 1 (VDDR1) and VDDR Type 2 (VDDR2). Both types lead to rickets, bone deformities, and other skeletal disorders in children, but they have different underlying causes and treatment approaches.

Ideally, the following investigations should be carried out for diagnosis and monitoring of therapy:

- Serum calcium and inorganic phosphate
- Serum alkaline phosphatase
- Serum 25-(OH) and 1,25-$(OH)_2$ vitamin D
- Parathyroid hormone level
- X-rays of affected bones
- Bone density scan
- Urine calcium assay
- Relevant genetic studies

VDDR Type 1 (VDDR1) - 1α-Hydroxylase Deficiency

VDDR1 is caused by mutations in the CYP27B1 gene, which leads to a deficiency in the enzyme that converts 25-hydroxyvitamin D (storage form) into its active form, 1,25-dihydroxyvitamin D (calcitriol). This results in decreased intestinal absorption of calcium and phosphate.

Treatment

1. Calcitriol supplementation: Since patients with VDDR1 cannot produce active vitamin D, they are treated with calcitriol (1,25-dihydroxyvitamin D) directly. This bypasses the enzymatic defect and helps maintain normal calcium and phosphate levels. Dosing is individualized, starting at 0.5-1.0mcg/day, with adjustments based on biochemical response.
2. Calcium and phosphate supplementation: In some cases, additional calcium and phosphate may be needed to normalize serum levels, as calcitriol increases their absorption from the intestine. Oral calcium, typically as carbonate or citrate is given (500-1000mg/day), depending on age and dietary intake.
3. Dietary management: Diet rich in calcium and vitamin D – dairy products, leafy greens, fortified foods.
4. Monitoring: Regular monitoring of serum levels of calcium, phosphate, and alkaline phosphatase is essential to prevent complications such as hypercalcaemia and hypercalciuria, which can occur if treatment is not appropriately adjusted. Growth and development assessments should be routine.

Most children respond well to treatment with calcitriol and calcium, and bone deformities improve over time with early intervention.

VDDR Type 2 (VDDR2) - Hereditary Vitamin D-Resistant Rickets (HVDRR)

VDDR2 is caused by mutations in the vitamin D receptor (VDR) gene, leading to an inability of target tissues to respond to the active form of vitamin D. Laboratory investigations reveal low serum 1,25 $(OH)_2$ vitamin D with often normal levels of 25(OH)vitamin D, high alkaline phosphatase, and elevated Parathormone (PTH).

Treatment

1. High doses of calcitriol: Since VDDR2 involves resistance to vitamin D, much higher doses of calcitriol are often required (starting from 1-3mcg/day) to stimulate even a partial response from the mutated vitamin D receptor. However, responsiveness can vary depending on the mutation.
2. High doses of oral calcium: Large doses of calcium may be necessary to improve calcium absorption and prevent hypocalcaemia. In severe cases, intravenous calcium infusions may be needed.
3. Phosphate supplementation: As in VDDR1, phosphate supplementation is sometimes required.
4. Diet: Balanced diet rich in vitamin D and Calcium.
5. Long-term care: In severe cases, the skeletal deformities may not fully resolve, even with treatment. Physical therapy or orthopaedic interventions may be needed to address skeletal abnormalities.

Unlike VDDR1, VDDR2 can be more difficult to manage due to the variable response to treatment and the severity of the mutations in the VDR gene. Some children with severe VDR mutations may have poor treatment outcomes.

Prognosis

- VDDR1: With early diagnosis and appropriate treatment, children with VDDR1 typically have a good

prognosis, with improved growth and resolution of rickets.

- VDDR2: The prognosis can be more variable. While some children respond to high-dose treatment, others may continue to experience skeletal deformities and impaired growth. Additionally, some patients with VDDR2 can have non-skeletal symptoms, such as alopecia (hair loss), which does not respond to vitamin D treatment.

Monitoring and Long-term Management

-Regular blood tests to monitor calcium, phosphate, parathyroid hormone (PTH), and alkaline phosphatase levels.

-Regular bone density scans and X-rays to assess bone health and treatment efficacy.

-In cases where hypercalcaemia develops, treatment adjustments are made to avoid complications such as nephrocalcinosis (calcium deposits in the kidneys).

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EXCERPTS FROM THE 2024 PAN WEBINAR SERIES

Helicobacter pylori Infection in Paediatric Practice

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Introduction

- *Helicobacter pylori* is a Gram-negative bacterium that colonizes the mucous layer of the stomach and duodenum.
- *H. pylori* infection is chronic, persisting for many years if left untreated.
- About 50% of the world population are infected.
- The infection is acquired early in childhood.
- Early acquisition of H. pylori is associated with a higher risk of gastrointestinal disease.
- It is an important cause of peptic ulcer disease and gastric cancer, even though this is infrequent in children and adolescents.
- The majority of childhood infection is asymptomatic
- The infection is commoner in developing countries with poor hygiene, overcrowding and low socioeconomic class.
- The global prevalence of Helicobacter pylori infection ranges from less than 10% in developed countries to over 80% in developing countries.
- Eradication of the organism can be challenging due to a variety of reasons.
- Prompt and reliable diagnosis and strict adherence to prescribed medications are essential to successful eradication of this organism.

Structure of *H. pylori*

- *H. pylori* is an S-shaped bacterium measuring 0.5-5µm in length, with 5-7 polar sheathed flagella.
- The spiral shape and flagella are essential for colonization of the gastric and intestinal mucus.
- It is a Gram-negative bacteria with an outer and inner membranes separated by a periplasm of about 30nm in thickness.
- It has a dense cytoplasm containing nucleoid material and ribosomes.
- There is an electron-luscent area in the terminal region which is closely associated with a polar membrane where the flagella is inserted.
- The polar membrane is thought to be an assembly of ATPase molecules which generate energy for cell motility or cell wall synthesis.

Epidemiology

- A systematic review on the global prevalence of H. pylori infection in children showed a prevalence of 32.3%.
- Prevalence was higher in Low- and Medium-Income Countries (43.2%) in comparison with high income countries (21.7%).
- The prevalence was higher in older children; 41.6% in 13 – 18years, 33.9% in 7 – 12 years and 26% in 0 – 6 years.
- In Nigeria, there are regional differences in the prevalence.
- In the South-East, a prevalence of 36.3% was reported in children aged 6-12 years.
- In Owerri, South-east, prevalence was 20% in children 0.5 – 15 years.
- In Uyo, South-south, a prevalence of 30.9% was reported in children age 0.5-15 years.
- In Lagos, South-west a prevalence of 68.7% was found.
- A prevalence of 69% was reported in Northern Nigeria in children 0.5 – 10 years.

- Serology was used in most of the studies.
- Prevalence increased with age, highest among adolescents.
- H. pylori infection was significantly associated with poor sanitary conditions, low socioeconomic class, lack of potable water and poor sewage disposal system.

Risk factors

- Faeco-oral and oral-oral routes of transmission have been implicated.
- Person to person contact occur among close family members through sharing of utensils, food or drinks.
- Poor sanitation and hygienic practices facilitate transmission.
- Maternal to child transmission during pregnancy and child birth has also been postulated.

Pathogenesis

- Pathogenesis involves interplay of factors such as bacterial factors, host immune response and environmental factors.
- Once in the stomach, four steps are critical for *H.pylori* to establish colonization, persistent infection and disease in the host.

i. Survival of the organism in an acidic medium
ii. Motility with the aid of the flagella to reach the host epithelial cells
iii. Attachment with bacterial adhesins to the host receptor cells
iv. Tissue injury through toxins

Key factors implicated in the pathogenesis of *H. pylori:*

- Urease enzyme
- Flagella
- Adhesins – Heat shock proteins, Neutrophil-associated proteins, sialic acid binding proteins, blood group antigen binding proteins
- Virulence factors – cytoxin-associated gene A (VagA) vacuolating cytotoxin A (VacA), outer membrane proteins and lipopolysaccharides.

These factors disrupt the integrity of the gastric mucosal leading to epithelial cell damage, inflammation and ulceration.

Clinical features

- Majority of children are asymptomatic
- Atrophic gastritis
- Peptic ulcer disease – causes about 80% of gastric ulcer and 90% of duodenal ulcer
- Mucosa-associated lymphoid tissue (MALT) lymphoma Gastric cancer
- Extra-gastric complications – iron deficiency anaemia, immune thrombocytopaenic purpura, short stature,
- Peptic ulcer disease
- Epigastric pain – related to feed.
- Haematemesis
- Melena

RED FLAG MISSION

- Localized epigastric pain
- Right upper or lower quadrant pain
- Dysphagia
- Unintentional weight loss
- Decelerating linear growth
- Delayed puberty
- Unexplained fever
- Family history of Inflammatory Bowel Disease, Celiac disease, Peptic ulcer disease
- Odynophagia
- Persistent vomiting
- Overt GI bleed

DIAGNOSIS

Invasive

- Endoscopy
- Histology
- Rapid urease test
- Culture

Non-invasive

- Urea breath test (UBT)
- Stool antigen test

- Culture (stool)
- Molecular test
- Serology (urine saliva)
- Endoscopy

❖ Antral nodularity – sensitivity (39.5% - 96.4%), specificity (83.6% - 96.4%)

❖ Erythema
❖ Erosions
❖ Thickened folds or absence of rugae
❖ Mosaic appearance
❖ Visible submucosal vessels
❖ Gastric black spots

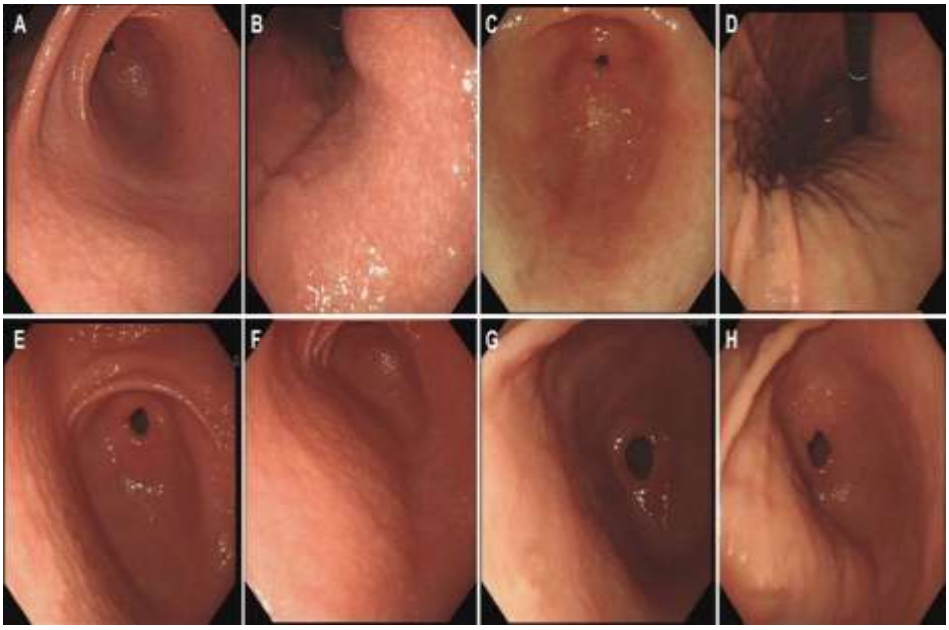

Figure 4: Endoscopic findings in patients with PUD

Histology

- It is the gold standard for the diagnosis.
- Sensitivity 95%, specificity 98%
- Two specimens from the antrum, one from the gastric angulus and two from the corpus

Findings

- Atrophic gastritis
- Intestinal metaplasia

Rapid Urease test

- Preformed urease in biopsy specimen releases ammonia from the urea containing medium
- Two samples collected from the antrum and corpus

Advantages – rapid, easy to perform, inexpensive, highly specific.

- ***Limitations***
  -Requires high density of bacteria
  -False negative result with use of PPI, antibiotic
  -False positive from urease positive bacteria – proteus, staphylococcus, klebsiella

- Culture of biopsy specimen
- Culture of H. pylori
- Organism genotyping
- Antimicrobial sensitivity
- Samples should be sent within 30mins of collection
- It has low sensitivity but high specificity compared with histology
- PPI and antibiotic affect yield.
- Urea Breath test
- Substrate containing urea enriched with carbon isotope is ingested (13C or 14C)

- Breath exhaled samples are collected before and after ingestion of urea substrate
- Has sensitivity of 95% and specificity 95% - 100%
- Used in initial diagnosis and confirmation of eradication

Limitations

-Cannot be used in children less than 6 years.
-Use of PPI, antibiotic affects results.
-It is expensive.

Stool antigen tests

-The antigen from *H. pylori* is detected by ELISA.
-Two step monoclonal antigen test is preferable to polyclonal.
-Has a sensitivity of 93% and specificity of 96%.

Limitations

-False negative result with use of PPI, antibiotic and bismuth.
-Molecular test.
-Biopsy and other specimens can be used.
-PCR, FISH.
-Useful in antimicrobial sensitivity.
-PCR has an advantage over histology and RUT in patients with bleeding PUD.

Serology

- Detection of serum IgG antibodies against *H. pylori*
- Cannot distinguish previous from current infection
- Antibodies against certain *H. pylori* proteins CagA, VacA, GroEI indicates active infection

Others

- Test on plasma, blood, saliva, urine using Gastropanel to detect H. pylori antibodies and pepsinogen I, pepsinogen II and gastrin-17.
- Able to predict *H. pylori* infection and atrophic gastritis with a likelihood of 90% - 95%.

Differential diagnoses

- Other causes of gastritis and PUD – ingestion of NSAIDS
- Gastroesophageal reflux disease
- Functional dyspepsia
- Inflammatory bowel disease
- Celiac disease
- Pancreatitis

TREATMENT

JOINT ESPGHAN/NASPGHAN GUIDELINES ON TREATMENT OF *H. PYLORI*

- Invasive investigative procedures only if treatment will be offered for positive results.
- Aim at 90% eradication with initial treatment.
- Strict adherence to treatment.
- Use clarithromycin only in susceptible strains.
- High dose of PPI, amoxicillin and metronidazole for 14 days of bismuth quadruple should be used where susceptibility profiles are unavailable.
- Success of therapy should be confirmed 4 – 8 weeks after treatment using reliable non-invasive tests.
- Test and treat strategy should be discouraged.
- Testing should be discouraged in functional abdominal pain.
- Non-invasive study for children with chronic ITP.

-Treatment should be based on antimicrobial susceptibility.
-A combination of proton pump inhibitors such as omeprazole, rabeprazole, esomeprazole and antibiotics – clarithromycin, amoxicillin, metronidazole and tetracycline.
-Resistance to clarithromycin and metronidazole are on the increase.

Treatment option

1. Susceptible to CLA and MET.
2. Resistant to CLA but susceptible to MET.
3. Resistant to MET but susceptible to CLA.
4. Resistant to CLA and MET.
5. Unknown resistance status.

Other options

1. PPI, AMO, CLA for 14days, sequential
2. PPI, MET, AMO or bismuth quadruple
3. PPI, AMO, CLA or bismuth quadruple
4. PPI, AMO (high dose), MET or bismuth quadruple
5. PPI, high dose (AMO) MET or bismuth based

Initial treatment

-Amoxicillin, CLA
-Amoxicillin, MET
-Sequential

Second line treatment

-Amoxicillin, MET
-Amoxicillin, CLA
-Endoscopy and individualized susceptibility regimen
-Bismuth quadruple
-PPI, high dose AMO, MET

Prevention

- Environmental sanitation, hand washing, provision potable water.
- Health education, vaccination
- Detect early detection of the infection and prompt treatment if indicated. Adherence to treatment.
- Re-evaluation after treatment to ensure eradication.
- Endoscopy to detect early stage of gastric cancer.

Table 1: Treatment regimen

Drug	Body weight(kg)	Morning dose	Evening dose
PPI	15 – 24	20mg	20mg
	25–34	30mg	30mg
	≥35	40mg	40mg
Amoxicillin	15 – 24	500mg	500mg
	25–34	750mg	750mg
	≥35	1000mg	1000mg
Clarithromycin	15 – 24	250mg	250mg
	25–34	500mg	250mg
	≥35	500mg	500mg
Metronidazole	15 – 24	250mg	250mg
	25–34	500mg	250mg
	≥35	500mg	500mg
Bismuth	<10yrs	262 QID	
	≥10yrs	524QID	

Challenges

- Diagnostic challenge – lack of facilities such as endoscopy
- Antimicrobial sensitivity pattern is unknown
- Treatment administered without any test done to confirm H. Pylori infection
- Poor adherence to treatment
- Post-treatment confirmation of eradication not usually done
- Absence of guidelines for testing and treatment.

Conclusions

- Helicobacter pylori is a Gram-negative bacteria commoner in developing countries.
- Infection is acquired during childhood and persists for many years if left untreated.
- Majority of infected persons are asymptomatic while others can develop peptic ulcer disease, MALT lymphoma and gastric cancer.
- Various diagnostic tools are available but histology of specimen obtained during endoscopy is the gold standard.
- Triple therapy with a PPI and two antibiotics is advocated with strict adherence

Recommendations

- Proper evaluation of patients before testing.
- Stool antigen test OR Urea breath test as the initial investigation.
- Discourage treatment with triple regimen without a positive test for *H. pylori.*
- Counselling of patient/parents on side effects of drugs to be used and strict adherence to treatment.
- Mandatory confirmatory test 4 – 6weeks after treatment.
- Studies on antibiotic sensitivities to current antibiotics.
- National guidelines on testing/treatment of *H. pylori* by NAPGHAN.

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Questions

1. Which of the tests below diagnose helicobacter pylori infection more accurately?

a. Endoscopy
b. Histology
c. Rapid urease test
d. Culture
e. Molecular test

2. Which of the following is INCORRECT concerning helicobacter pylori infection?

a. Commoner in developing countries
b. Acquisition occurs in early childhood
c. Prevalence is higher in early childhood
d. Majority of infected persons are asymptomatic
e. It is the commonest cause of peptic ulcer disease

3. The attachment of helicobacter pylori is facilitated by these proteins EXCEPT

a. Heat shock proteins
b. Neutrophil associated proteins
c. Sialic acid binding protein
d. Blood group antigen binding protein
e. Epithelial cell binding protein

4. A 10year old girl presented with abdominal pain which is located in the epigastric region. She had stool antigen test which was positive but antimicrobial susceptibility could not be done. Which of the following combination should be prescribed?

a. Omeprazole, amoxicillin, metronidazole
b. Omeprazole, amoxicillin, clarithromycin
c. Omeprazole, metronidazole, clarithromycin
d. Omeprazole, clarithromycin, bismuth, amoxicillin
e. omeprazole, amoxicillin, metronidazole, clarithromycin

5. Which of these diagnostic tools for helicobacter pylori is NOT recommended in under-fives?

a. Urea breath test
b. Serology
c. Endoscopy
d. Rapid urease test
e. Stool antigen test

Key to the questions

1	2	3	4	5
B	C	E	A	A

Management of Childhood Hypothyroidism in Primary Care Setting in Nigeria

Subtitle: Strategies for Effective Diagnosis and Treatment

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Introduction

Hypothyroidism is reduced thyroid hormone in the system from structural or functional defects

- Congenital Hypothyroidism is the most common preventable cause of neurocognitive disability and is the most common disorder diagnosed through newborn screening.
  -Permanent
  -Transient
- Acquired Hypothyroidism occurs after birth and may be due to Autoimmune disorders, iodine deficiency, radiation therapy, certain medications

Permanent

Transient

Clinical features of Childhood Hypothyroidism

Newborn period

-Poor feeding,
-Somnolence,
-Reduced activities,
-Prolonged jaundice,
-Constipation,
-Umbilical hernia,
-Relative macroglossia,
-Hoarse cry,
-Large fontanelles,
-Hypotonia,
-Cold and
-Mottled skin

Childhood

-Growth failure (linear),
-Obesity,
-Slow cognitive and intellectual abilities,
-Delayed tooth eruptions,
-Puffy face,
-Coarse brittle hair,

-Primary congenital hypothyroidism is a defect in the thyroid gland's ability to produce thyroxin which may be structural or functional
-It is the commonest cause of CH in world with a prevalence of 1 in 2,500 live births
-It is mostly detected during routine newborn screening in Europe and America and parts of Asia
-Severity of the disorder is manifested in reduced neurocognitive development

Permanent Congenital Hypothyroidism

-It is common
-To prevent mental retardation, the diagnosis must be made early, preferably within the first few days of life; at that age, clinical recognition is difficult if not impossible;
-Sensitive, specific screening tests
-Simple, cheap effective treatment are available; and
-the benefit-cost ratio is highly favourable
-Fatigue,
-Cold intolerance,
-Delayed puberty

Adolescence

-Delayed puberty.
-Menstrual irregularities.
-Obesity.
-Depression and mood swings.
-Poor academic performance.
-Fatigue and lethargy.

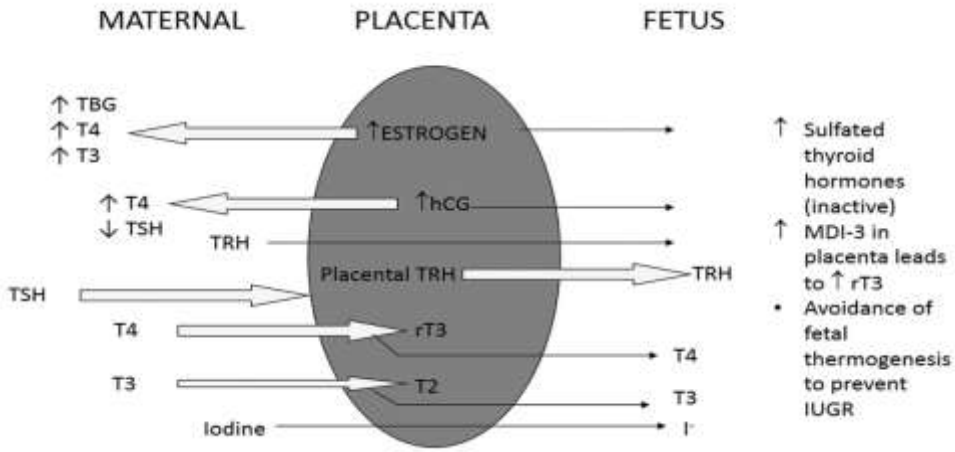
Clinical Examination

- Importance of Detailed History
- X-ray the knee – failure of one or both epiphyses to appear reflects intra uterine hypothyroidism
- Radio isotope study and/or ultrasound

Interpretations of Thyroid Function test

- Elevated TSH and Low Free T4: Primary Hypothyroidism

- Low TSH and Low Free T4: Central Hypothyroidism
- Elevated TSH and Normal Free T4: Subclinical Hypothyroidism
- Clinical Features Correlated with TFTs



Maturation of the hypothalamic- pituitary-thyroid (HPT) axis starts around 20 weeks and is complete only close to term. Foetal iodine deficiency, Thyrotropin receptor blocking antibodies, intra uterine exposure to antithyroid drugs
Figure 1: Schematic diagram showing maternal-placental-foetal thyroid interactions

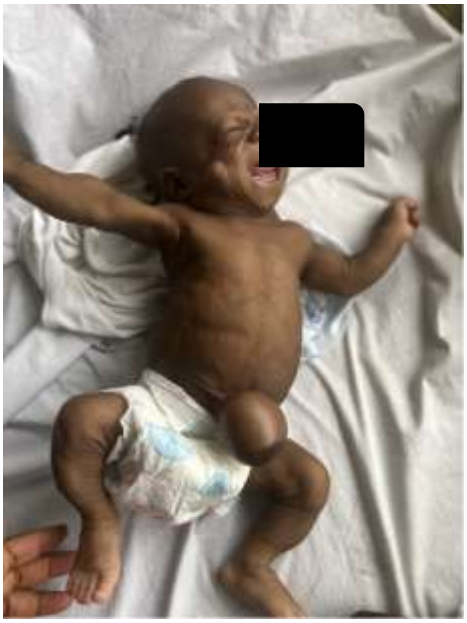


Figure 1: Newborn with hypothyroidism

Management Strategies

- Levothyroxine Therapy: Dosage and Administration.
- Monitoring and Follow-Up.
- Addressing Nutritional Deficiencies.
- Well children with normal f T4 and venous TSH 6 - 20 mU/L may be observed initially, and thyroid imaging should be performed.
- If, however, TSH elevation >10 mU/L in the next test, start L-Thyroxin treatment. Children with features of CH and TSH is > 20mIU/L, start Thyroxin immediately.
- L-Thyroxin can be administered as crushed tablets, mixed with a few millilitres of water, breast or formula milk and given via a spoon or syringe.
- The initial dose of L- Thyroxin should be 10 - 15 ug/kg per day depending on the severity of the hypothyroidism.
- The smallest tablet is 25 ug, but this can be halved.

The aim of treatment is to normalize freeT4 and TSH within two weeks if possible, to give a better neurodevelopmental outcome.

Levothyroxine Therapy: Dosage and Administration

- Monitoring and Follow-Up care.

- Addressing Nutritional Deficiencies every three months in the first year and bi- yearly after for 3 years.
- If the TSH is > 5 mU/L and the free-T4 level is in the lower half of the normal range or below the normal range, then the dose should be raised by 12.5-25 ug per day and the TFTs should be repeated in 4 – 6 weeks
- Conversely, the dose should be reduced by a similar amount if the TSH level is < 0.5 mU/L.

Table II: Thyroid Function Tests and interpretations

TSH (mU/L)	Free T4 (ng/dL)	Free T3 (pg/mL)	Interpretation	Clinical Features
25 0.6 - 5.5	0.5 (0.8 - 2.0)	1.8 (2.3 - 4.2)	Primary Hypothyroidism	Fatigue, weight gain, cold intolerance, dry skin, growth retardation
9.8 0.6 - 5.5	1.6 (0.8 - 2.0)	2.6 (2.3 - 4.2)	Subclinical Hypothyroidism	Often asymptomatic or mild symptoms: fatigue, weight gain
5.1 (0.6-5.5)	2.4 (0.8 - 2.0)	4.9 (2.3 - 4.2)	TSH-producing Pituitary Adenoma	Symptoms of hyperthyroidism: weight loss, heat intolerance, palpitations
0.3 (0.6-5.5)	0.6 (0.8 - 2.0)	1.9 (2.3 - 4.2)	Central Hypothyroidism	Similar to primary hypothyroidism: fatigue, weight gain, cold intolerance
0.1 (0.6-5.5)	4.3 (0.8 - 2.0)	4.6 (2.3 - 4.2)	Thyrotoxicosis (Graves' Disease, Exogenous Thyroid Hormone)	Weight loss, heat intolerance, palpitations, tremors
5.4 (0.6-5.5)	0.6 (0.8 - 2.0)	1.3 (2.3 - 4.2)	Non-thyroidal Illness (Euthyroid Sick Syndrome)	Symptoms related to underlying illness rather than thyroid dysfunction
2.0 (0.6-5.5)	1.4 (0.8 - 2.0)	4.0 (2.3 - 4.2)	Euthyroid	No thyroid dysfunction; symptoms may be due to non-thyroidal causes

Hashimoto Thyroiditis

- Is the most common cause of acquired hypothyroidism in the world, as iodine deficiency is now being eradicated.
- It is more common in girls, particularly in adolescence, and there is a family history in one-third of cases.
- 8-year-old girl presented to the Consultant clinic with history of neck swelling, and weakness for the past 3 months. There was no other symptom Examination did not yield any other abnormality.
  Thyroid function test showed:
  -TSH 5.03 uIU/mL (0.34–5.5),
  -fT4 0.3 ng/dL (0.58–1.2),
  -fT3 3.3 pg/mL (2.5–3.9)
  -Thyroglobulin antibody and thyroid peroxidase antibody were negative, urine iodine 30.8 ug/L (<100 ug/L)
- Thyroid scan only showed enlarged goitre.
  Commenced iodine (2 -3 drops thrice daily for 1 month).
  Re assessed 1.5 years after (lost to follow up).
  Goitre had increased in size with symptoms suggestive of hyperthyroidism
  -TSH 8.05 uIU/mL (0.34–5.5),
  -fT3. 2.8 ug/dL, (2.5–3.9)
  -fT4. 5.2 ng/dL (0.58–1.2)
  Interval information revealed non-compliance with iodine regimen.
  Repeat anti-TPO antibody was elevated above normal
  Commenced L-thyroxin at 5ug/kg/day and it has been a yoyo since then

Hashimoto Thyroiditis in Down Syndrome

- Commonest endocrine disorder in Down's syndrome

- Most commonly subclinical hypothyroidism
- The incidence of hypothyroidism in Down's syndrome in our clinic is 2%
- Because of its prevalence, we check TFT in all children with DS
  TSH 12.05 uIU/mL (0.34–5.5), fT3. 2.8 ug/dL, (2.5–3.9)

- **Subclinical hypothyroidism**
  -fT4. 1.0 ng/dL (0.58–1.2).
  -Treat or not treat?
  -We strive to normalise TSH even if we get higher levels of fT4 and fT3.
  -Most mothers report better motor function in their babies.

Challenges in Primary Care Setting

- Limited Access to Diagnostic Tools.
- Lack of Awareness and Training among Healthcare Providers.
- Socioeconomic factors.

Recommendations for Improvement

- Training Programmes for Primary Care Providers
- Establishing Screening Programmes
- Public Health Education Campaigns
- Improving Access to Diagnostic Facilities

Conclusions

- Hypothyroidism is common and easily treatable.
- Starting a newborn screening is still possible and must be emphasised to prevent serious debilitating consequences.
- Training primary care physicians and health workers to recognise and start treatment or refer as quickly as possible.

Questions on Management of Hypothyroidism in the Primary Care setting.

1. In the management of congenital hypothyroidism, what is the primary goal of initiating early treatment with L-Thyroxin?

a. To normalize Free T3 levels within 2 weeks
b. To achieve optimal neurodevelopmental outcomes by normalizing Free T4 and TSH levels within 2 weeks
c. To reduce the size of the thyroid gland within 2 weeks
d. To eliminate all symptoms of hypothyroidism within 2 weeks

2. What is the significance of elevated TSH and normal Free T4 levels in the context of thyroid function tests?

a. Central Hypothyroidism
b. Subclinical Hypothyroidism
c. Non-thyroidal Illness
d. Primary Hypothyroidism

3. Which of the following is a recommended strategy for minimizing treatment failure in hypothyroidism management?

a. Increasing the dose of Levothyroxine regardless of TSH levels
b. Conducting regular follow-up and monitoring every three months in the first year
c. Using Thyroid Stimulating Hormone (TSH) levels alone to guide treatment
d. Discontinuing treatment if symptoms improve within the first month

4. In the primary care settings, what is the purpose of performing an X-ray of the knee in children suspected of hypothyroidism?

a. To assess the size of the thyroid gland
b. To evaluate growth retardation
c. To detect intrauterine hypothyroidism by the appearance of epiphyses
d. To rule out autoimmune thyroiditis

5. Which factor is most critical in differentiating transient from permanent congenital hypothyroidism?

a. Presence of maternal thyroid antibodies
b. Response to iodine supplementation
c. Results of thyroid ultrasound or radioisotope study
d. Initial TSH and Free T4 levels at birth

Key

Question	Correct options
1.	B
2.	B
3.	B
4.	C
5.	C

Comprehensive Clinical Management of Tuberculosis in Children

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Introduction

- Tuberculosis (TB) continues to impact the lives of millions of children globally.
- Unfortunately, < 50% of global childhood TB cases are notified by National TB Programmes (NTPs)
- Less than one-third of eligible under-5 TB contacts receive TPT,
- A huge diagnostic, treatment and prevention gap persists for childhood TB
- In Nigeria, only about 35% of estimated childhood cases are notified

Factors contributing to the low detection rate of Child TB

- Challenges with collecting suitable respiratory specimens, but stool specimen can now be tested
- Paucibacillary nature of TB in young children
- Lack of highly sensitive diagnostic tests
- Overlap of symptoms with other childhood diseases, leading to misdiagnosis

Factors that increase the risk of TB in Children

- Young age < 5 years
- Household or other close contacts with a TB case
- Severe undernutrition
- HIV infection
- Malignancies like Leukaemia and Lymphoma
- Other infectious disease like measles and pertussis
- Chronic malabsorption syndrome
- Diabetes mellitus

Common sites of TB disease in Children (Pulmonary and Extra pulmonary)

- Lungs (predominant)
- Lymph nodes
- Central nervous system
- Disseminated/miliary
- Bones and joints
- Pleura
- Genitourinary system

Diagnostic Evaluation of Child TB

- TB diagnosis in children relies on a combination of the following:
- Careful history, including symptoms consistent with TB
- History of contact especially in the past 12 months
- Careful clinical examination, including growth assessment
- HIV testing (if status unknown)

Bacteriologic confirmation

- CXR (preferably AP and lateral for under-fives and PA in older children)
- Other investigations relevant for site of presumed EPTB
- Bacteriologic confirmation of TB
- Though bacteriologic confirmation in children with presumed TB is 30% - 40%
- Efforts should be made at bacteriologic diagnosis in children with presumed TB
- Clinical diagnosis by a trained HCW is very useful in childhood TB diagnosis
- Treatment should not be delayed on account of negative bacteriologic test when there is strong clinical evidence in support of TB diagnosis
- First line tests: molecular WHO-approved rapid diagnostic tests (mWRDs)
  Xpert MTB/RIF, Xpert MTB/RIF Ultra assay, and Truenat MTB, MTB Plus and MTB-RIF Dx assay
- Tests for diagnosis of TB without drug resistance detection (WRDs)

- Loop-mediated isothermal amplification (TB-LAMP)
- Urine lateral flow lipoarabinomannan assay (LF-LAM) for HIV positive cases
- Follow-on diagnostic tests for detection of additional drug resistance
  NAATs for detection of resistance to 2nd line drugs (Xpert MTB/XDR Assay)
- Line-probe assays (LPAs)

Roles of Chest Radiographs in TB diagnosis

- Assists in TB diagnosis where bacteriologic test is negative or not feasible.
- Used in categorising TB according to disease severity
- CXR features suggestive of TB include:
- Enlarged perihilar or paratracheal lymph nodes;
- dense alveolar opacification
- miliary pattern of opacification
- cavitation especially in older adolescents
- Pleural or pericardial effusion

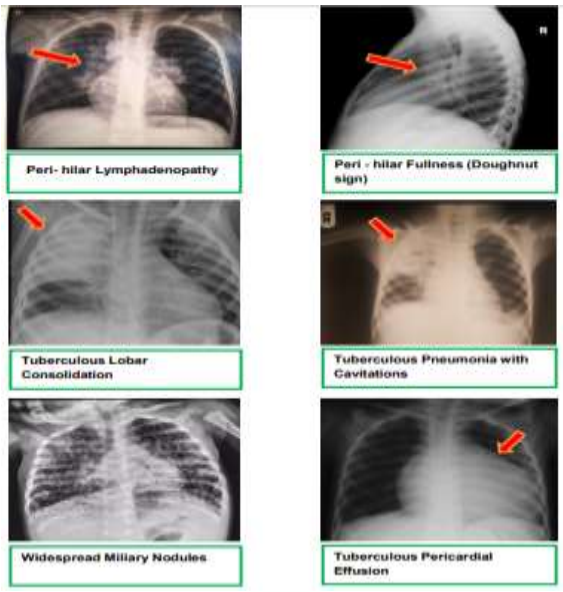

Figure 1: Some chest radiographic features of childhood TB

Other Important Considerations in PTB Diagnosis

- After diagnosis, 2 important evaluations must be made to inform choice of regimen Assess for risk for DR-TB:
- Bacteriologic confirmation of DR-TB
- Contact with a person presumed or confirmed to have DR-TB case
- Previous TB treatment in the past 12 months
- Determine whether the child has severe or non-severe disease to inform selection of treatment regimen using CXR findings.

Table I: Determination of the severity of PTB

Non severe PTB	Severe PTB
Intra-thoracic lymph node TB without airway obstruction	Presence of cavities
***Paucibacillary, non-cavitary disease confined to one lobe of the lungs and without a miliary pattern**	Bilateral lung disease

***Consider paucibacillary disease if Gene Xpert test is negative, trace, low or very low**

Breastfeeding recommended despite mother's TB status

Management of Drug Resistant TB (DRT)

- Diagnosis of DR-TB is based on Bacteriologic confirmation
  AND/OR
- Clinical diagnosis by documenting any of the followings:

Source case with presumed or bacteriologically confirmed DR-TB

- No response to first-line regimen after 2–3 months despite good adherence.

- Recurrence of TB disease within 12 months of completed treatment.

Treatment regimen for DR-TB.

- Isoniazid mono-resistant TB: 6 months course of rifampicin, Pyrazinamide, ethambutol and levofloxacin.
- Multi-drug Resistant and Rifampicin Resistant (MDR/RR-TB) TB in children 0 - < 14 year.

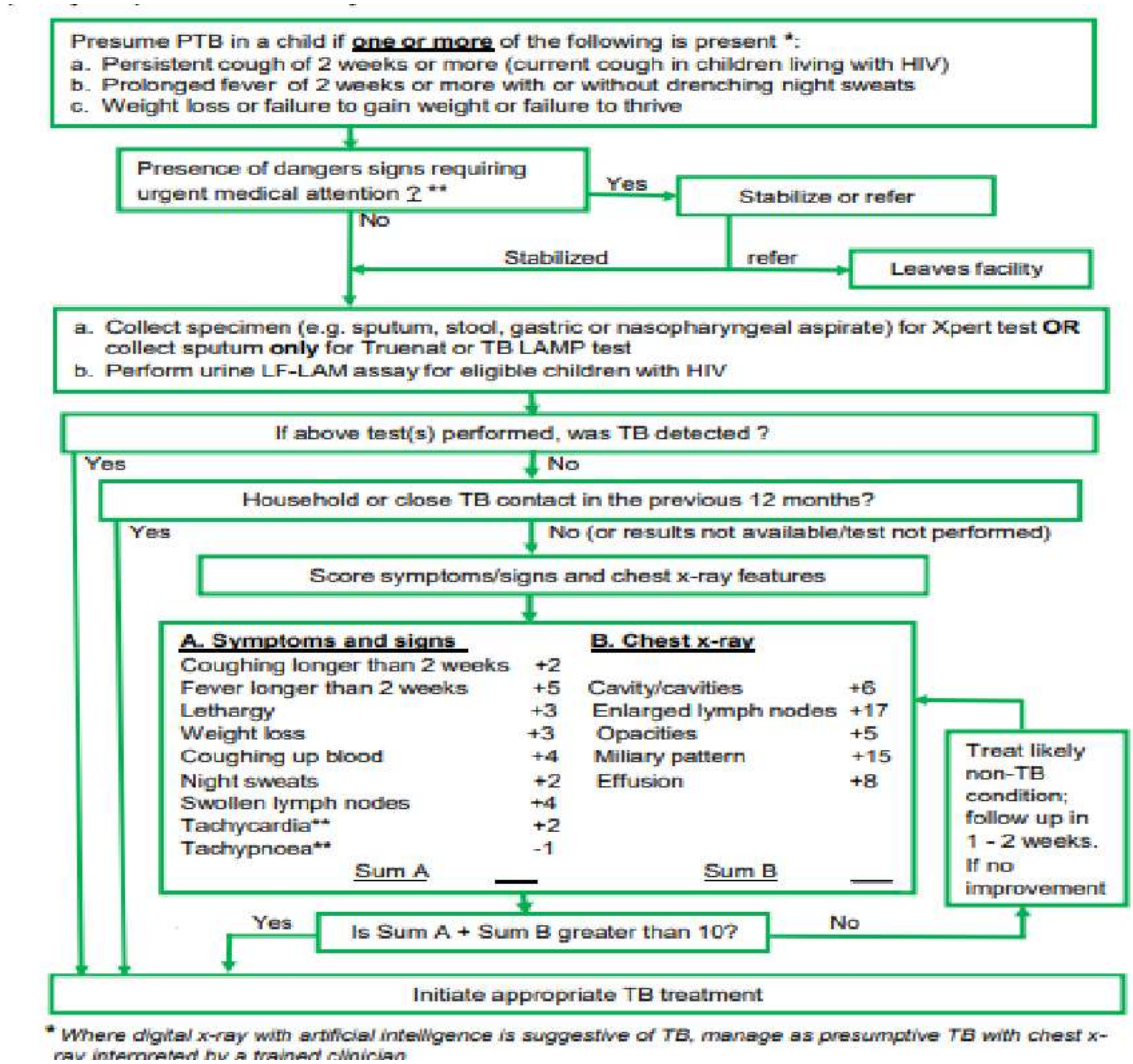

Figure 2: Algorithm A: Facility based diagnostic Algorithm for Drug Susceptible and Drug Resistant PTB in Children < 10 years old where chest x-ray is available

In Advanced retroviral disease, start ART within 7 days of commencing TB treatment but monitor for Immune Reconstitution Inflammation Syndrome (IRIS).

Adjuvant therapy in TB treatment

- Steroids: indicated in TBM, TB pericarditis, TB lymph node with pressure effect.

Oral Prednisolone 2 mg/kg/day (max 60 mg/day) for 4 weeks. Taper gradually over 2–4 weeks.

- Dexamethasone 0.3–0.6 mg/kg/day given in the same pattern as prednisolone.
- Pyridoxine (vitamin B6): for malnourished and HIV-positive children, and adolescents to protect against INH-induced peripheral

neuropathy. Oral 12.5mg daily for children < 4 years and 25mg daily for children ≥ 4 years.

Contact investigation and management

- Process of identifying individuals with TB disease or LTBI among contacts of TB patients.
- Anyone who shares enclosed living space for ≥ one nights or for extended periods during the day within 3 months preceding treatment initiation is considered close contact.
- Contact investigation is highly prioritized due to its high yield and cost-effectiveness.
- It improves access to TPT, reduces disease transmission, and delay in treatment.

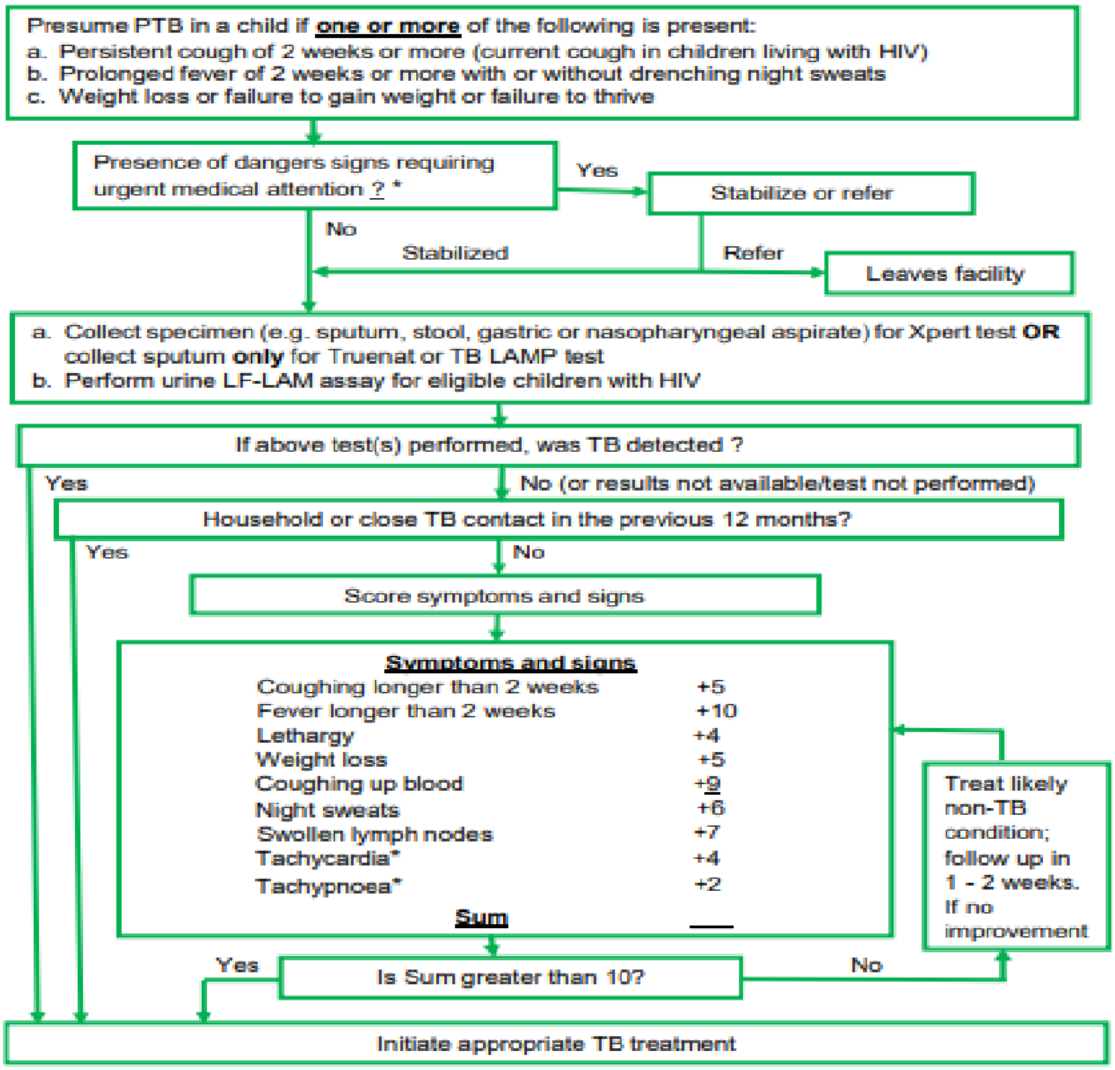

Figure 3: Algorithm B: Facility based diagnostic Algorithm for Drug Susceptible and Drug Resistant PTB in children < 10 years old where chest x-ray is not available. Adolescents are diagnosed using Adult Algorithm

The process of contact investigation and management includes the following:

- Record their details in "TB Contact Management Register".

- Conduct thorough clinical evaluation and testing (where possible) for them.
- Provision of appropriate TB treatment (TB treatment or TPT).

TB Preventive Therapy (TPT): LTB1 treatment

- All under-five and other eligible close contacts of bacteriologically confirmed PTB should receive TPT, irrespective of BCG vaccination status
- All PLHIV should receive TPT at ART initiation after ruling out active TB disease: Repeated courses no longer recommended
- Prior to TPT, rule out contraindications: (active TB disease, active hepatitis, peripheral neuropathy, hypersensitivity etc).
- Weigh patients every visit and adjust the dosage accordingly
- Monitor regularly for adherence and avoid treatment interruption
- Complete TPT card and update TB contact management register accordingly

TB Preventive therapy (TPT) in Children and Adolescents

- INH: daily for 6 months
- INH + Rifampicin (3HR): daily for 3 months
- INH + Rifapentine (3HP) - weekly for 3 months
- INH + Rifapentine (1HP) - daily for 1 month

Table II: Newly recommended treatment regimens for drug Susceptible PTB

Age/Weight (kg)	Type of PTB	Regimen in the treatment phases		Total duration	Notes
		Intensive	Continuation		
Infants < 3 months or weighing < 3 kg	All forms of PTB	2HRZE	4HR	6 months	
3 months to less than 12 years	Non-severe PTB	2HRZE	2HR	4 months	
	Severe PTB	2HRZE	4HR	6 months	Patients with severe acute malnutrition and those treated for TB in the past 2 years should be commenced on this regimen even if they have non-severe PTB.
12 - 15 years	Non-severe PTB	2HRZE	2HR	4 months	
	Severe PTB	2HRZE	4HR	6 months	Patients treated for TB in the past 2 years should be commenced on this regimen even if they have non-severe PTB
16 - 19 years	All forms of PTB (any severity)	2HRZE	4HR	6 months	16 - 19 years
12 - 19 years	All forms of PTB (any severity)	2HPZM	2HPM	4 months	Not recommended if less than 40kg and HIV positive with a CD4 cell count of less than 100 cells/mm^3

H - Isoniazid, R- Rifampicin, Z - Pyrazinamide, E - Ethambutol, P - Rifapentine, M - Moxifloxacin

-Where chest x-ray is not available treat with 6 months HRZE or HPZM regimen

Table III: Treatment regimen for Drug Susceptible Extrapulmonary TB

Age of patient	Type of EPTB	Regimen in the treatment phases		Total duration (months)
		Intensive	Continuation	
Infants < 3 months or weighing < 3 kg	Peripheral lymph node TB	2HRZE	4HR	6
3 months - < 16 years	Peripheral lymph node TB	2HRZE	2HR	4
≥ 16 years	Peripheral lymph node TB	2HRZE	4HR	6
0 - 19 years	All forms of EPTB except peripheral lymph node TB**, miliary TB, TB meningitis (TBM) and osteoarticular TB	2HRZE	4HR	6
	Osteoarticular TB	2HRZE	10HR	12
	Miliary TB	2HRZE	10HR	12
	TBM	2HRZE	10HR	12

** *Peripheral lymph node TB in ages 3 months to less than 16 years should receive 4 months regimen of RHZE*

Table IV: Treatment regimen for DR-TB

Fluoroquinolone susceptibility pattern	Regimen type
Fluoroquinolone susceptible	6 months of Bedaquilline, Levofloxacin, Clofazimine and Linezolid
Fluoroquinolone resistant	6 months of Bedaquilline, Delamanid, Clofazimine and Linezolid

- Adolescents ≥ 15 years should be treated with adult DR-TB regimens

Table V: Management of TB/HIV co-infections

TPT-2: Management of newborn infant of a mother with TB disease

- Ensure mother receives effective TB treatment, to reduce transmission risk.
- If the newborn is without any features of active TB disease, provide TPT.
- Delay BCG vaccination until two weeks after TPT.
- Daily INH for 6 months is preferred in HIV-exposed infant on Nevirapine prophylaxis.
- On completion of TPT, do Mantoux or Quantiferon TB gold test.
- If the test is negative or not available, give BCG.
- If the test is positive, BCG not needed.

Conclusion

- TB remains a major threat to children, especially in high burden countries like Nigeria
- Most childhood TB cases are undetected and untreated and most children who are eligible for TPT do not benefit from it
- A comprehensive approach focusing on thorough clinical evaluation of presumed cases, timely diagnosis/treatment, thorough contact investigation and TPT are crucial in reducing the impact of childhood TB
- Every missed case is a missed opportunity to prevent further transmission and death

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S/N	Scenario	Action
1.	Child and adolescent diagnosed with TB/HIV co-infection at presentation	• Start TB treatment • Refer to ART clinic immediately ➢ At ART clinic: ✓ Initiate CPT ✓ Commence ART as soon as possible within 2 weeks of TB treatment initiation irrespective of CD4 count or WHO stage of disease *
2.	Known HIV-positive child and adolescent on ART, newly diagnosed with TB	• If on ART for less than 6 months, check for adherence to ART, offer counselling to clients and commence TB treatment immediately • If on ART for more than 6 months, rule out ART failure: ➢ Conduct viral load test ➢ Commence TB treatment, and if ART failure, manage with the appropriate ART regimen ➢ If no ART failure, continue ART but with modification of regimen as necessary and commence TB treatment ✓ If on dolutegravir (DTG) containing regimen, administer by doubling the dose of DTG ✓ If on raltegravir (RAL) containing regimen, replace RAL** with DTG (with appropriate dose adjustment) ✓ If on Lopinavir/ritonavir (LPV/r) based regimen, change regimen to DTG based regimen. Alternatively, super-boost ritonavir dose to achieve same dose as LPV in mg, in a ratio equal to or approaching 1:1 ✓ If on Atazanavir/ritonavir (ATV/r) or Darunavir/ritonavir (DRV/r) based regimen, replace ATV/r or DRV/r with DTG if DTG naive or with LPV/r if DTG-experienced (with appropriate dose adjustment).
3.	Child and adolescent on TB treatment diagnosed with HIV Infection	• Considering DTG or RAL containing regimen: ➢ Continue first-line TB medicines ➢ Double DTG or RAL dose (administer same DTG dose twice daily and double twice daily dose of RAL

** ART should be delayed at least for 4 weeks and initiated within 8 weeks after commencing treatment for TB meningitis*
*** Double the dosage of RAL for neonates instead of substituting with DTG.*

Questions on Comprehensive Clinical Management of Tuberculosis in Children

1. The 2022 notification rate of Child TB in Nigeria is:
   a. 5%
   b. 11%
   c. 35%
   d. 50%

2. Diagnosis of tuberculosis in children is best confirmed by:
   a. History and physical examination
   b. Chest radiography
   c. Tuberculin skin testing
   d. Xpert MTB Ultra
   e. Evidence of a positive adult contact with Tb

3. An 18-month-old boy presented to the Nutrition clinic weight loss and cough of 3 weeks duration. His mother is being managed for TB. Further evaluation of this child includes which of the followings:
   a. Sputum AFB, Chest Xray
   b. Mantoux test, Chest X-ray, ESR
   c. Stool Xpert MTB/Rif, Chest Xray
   d. Chest X-ray, Full blood count
   e. Urine TB LF-LAM, Stool Xpert MTB/Rif

4. The following indicate severe TB in children except:
   a. Single cavitary lesion on Chest X-ray
   b. Extrapulmonary lymph node TB
   c. Bilateral alveolar opacification
   d. One sided pleural effusion
   e. Single Intrathoracic lymph node TB with airway obstruction

5. Concerning tuberculosis in children:
   a. The absence of cavities on frontal chest X ray views rules out TB
   b. Demonstration of acid-fast bacilli is required to confirm Mycobacterium tuberculosis infection
   c. Stool specimen can now be used to test for TB using Xpert MTB/Rif
   d. TB adenitis is best managed by incision and drainage

e. Streptomycin is a component of the first line regimen

6. A 4-year-old boy who is a contact of his father who has TB presents to DOTs for contact investigation. In which of these scenarios will the child be ineligible for TB preventive therapy:

a. If he is asymptomatic
b. If his weight of 16kg
c. If his HIV test is reactive
d. If he has cough of 4 weeks
e. If the chest X-ray shows opacities

Key

Question	Correct options
1.	C
2.	D
3.	C
4.	B
5.	C
6.	A

Paediatric Acute Upper Airway Obstruction

Contemporary diagnostic considerations in the Nigerian Child

Ibraheem RM, Ayuk AC, Johnson WBR

Introduction

Anatomic considerations and aetiopathogenesis of Paediatric Upper Airway Obstruction

- Pediatric acute upper airway obstruction refers to a potentially life-threatening condition where there is partial or complete obstruction of the upper airway in children.
- This obstruction can occur at various levels of the upper respiratory tract
- May occur abruptly or over a gradual time course
- It leads to impaired airflow, which can result in significant respiratory distress, difficulty breathing, and in severe cases, hypoxia and respiratory failure.
- Respiratory tract is outlined by a continuous layer of mucosal surfaces from the nasopharynx to the lungs
- The respiratory tract can be divided based on an imaginary line through the thoracic inlet to differentiate upper from lower obstructive airway disorders

Nasal cavity

- The nasal cavity is divided into two nostrils by the nasal septum
- The nasal turbinates or choanae (superior, middle, and inferior) increase the surface area for humidifying and filtering air.
- The meati are spaces beneath each turbinate where the paranasal sinuses and nasolacrimal duct drain.
- The choanae connect the nasal cavity to the nasopharynx.

Pharynx

- The nasopharynx- receives the incoming air from the nasal cavity.
- The two eustachian tubes open into the nasopharynx and the pharyngeal tonsils lie at the back of the nasopharynx.
- The oropharynx-contains the palatine and lingual tonsils, receives air from the nasopharynx and food from the oral cavity.
- The laryngopharynx serves as a conduit for the simultaneous passage of food to the oesophagus, and air to the larynx.
- The retropharyngeal space lies between the posterior pharyngeal wall and the prevertebral layer of deep cervical fascia.
- It contains loose connective tissue and lymph nodes that drain the nasopharynx, paranasal sinuses, middle ear, teeth, and adjacent bones.
- The space extends from the base of the skull down to vertebra C7 or T1.

Larynx

- The larynx consists of nine pieces of cartilage joined by membranes and ligaments.
- The epiglottis covers the glottis during swallowing to prevent the entrance of food.
- The thyroid cartilage protects the front of the larynx.
- The larynx houses the vocal cords and serves as a gateway to the lower airway.
- Crucial in maintaining airway patency.

Trachea

- The trachea is a flexible tube consisting of four layers.
- The mucosa with cilia that sweeps debris away from the lungs toward the pharynx.
- The submucosa layer.
- Hyaline cartilage forms 16 to 20 C-shaped rings that wrap around the submucosa and prevent the trachea from collapsing during inspiration.
- the outermost layer is the adventitia.
- The trachea bifurcates at the carina into the right and left mainstem bronchi.
- Part of the trachea is outside the thoracic cavity.

Why are children prone to Upper Obstructive Airway Disorders?

The vulnerability of the upper airway of children to obstructive lesions can be partly explained by-

- The laws governing air and fluid dynamics.
- The anatomic peculiarities of the airways of infants and young children.
- The "relative immunological immaturity" of infants and young children predisposing to infective lesions

The law governing air and fluid dynamics

- Some negative pressure is exerted on the upper airway walls by a laminar column of air-flow normally.
- Inflammatory narrowing causes an increase in the airflow through the narrowed segment, resulting in negative pressure within the lumen (Venturi effect).
- As a consequence, there is an obstruction-related reduction in the pressure exerted on the extrathoracic airway wall (Bernoulli principle),
- Resultant enhancement of the obstructive lesion by further inward collapse in the extrathoracic airway segment, turbulent airflow and the generation of the stridulent sound.
- Stridor, a sound resulting from rapid turbulent flow of air through a narrowed part of the upper airway
- It is most audible when the obstruction is located in the laryngopharynx, larynx, or the extrathoracic trachea.
- The sound is more often inspiratory and of a medium or low-pitch quality
- A loud inspiratory stridor is regarded as a localizing feature of a subglottic lesion
- With disease progression, the stridulent sound may however be softer and bi-phasic (inspiratory and expiratory).
- Resistance – the inherent capacity of the airways and tissues to oppose airflow towards the lungs.
- Airflow resistance is inversely proportional to the fourth power of the radius of a "tube" (Poiseuille's law)
- If the airway lumen is decreased by half, there is a corresponding 16-fold increase in the resistance.
- Newborns and infants with their smaller airways are prone to marked increase in airway resistance from inflamed tissues and secretions.

Anatomic Reasons

- Narrower airways of infants and children compared with adult's, ideal for the Poiseuille's law.
- Loose submucosal attachment at epiglottis and subglottis, prone to rapid oedema.
- The submucosal tissue vascularity increases propensity for subglottic oedema (from infective triggers)
- Abundant mucous membrane and glands in extrathoracic airway.
- The high and vertical position of the epiglottis with the loosely attached submucosa.
- A soft and less stiff cartilaginous framework predisposed to dynamic collapse during inspiration.
- A relatively big size of the infant's tongue to the oropharynx.

Immunological immaturity

- "Immunological immaturity" refers to the incomplete development of the immune system in infants and young children.
- This immaturity can predispose them to various infective lesions or infections.

Reasons for increased risks for infections

- Decreased Antibody Production
- Limited Cell-Mediated Immunity
- Reduced Complement Activity
- Immature Phagocytic Function
- Thymus and Lymphoid Tissue Development
- Exposure to Novel Pathogens: Constant exposure to new microbes as they explore their environment

Aetiology of Upper Airway Obstruction (UAO)

-Acute or Chronic-
Further subdivided as:
-Congenital /Acquired
-Infectious/Non-infectious
-Supraglottic/subglottic

Congenital causes

- Choanal atresia
- Laryngomalacia
- Laryngeal web
- Laryngeal stenosis
- Laryngocele
- Tracheomalacia
- Craniofacial anomalies (e.g., Pierre–Robin sequence)
- Dysmorphic syndromes (e.g., Crouzon syndrome, Treacher–Collins syndrome)
- Vascular rings
- Double aortic arch
- Hemangiomas

Acquired

Infectious

- Viral croup,
- Epiglottitis,
- Retro/lateral pharyngeal abscess,
- Peritonsillar abscess,
- Bacterial tracheitis,
- Laryngeal or faucial diphtheria
- Severe pharyngotonsillits

Non-Infectious

- Burns- caustic or thermal
- Foreign body aspiration
- Airway trauma (penetrating/ blunt)
- Airway burns (caustic/ thermal)
- Allergy
- Vocal cord paralysis/dysfunction
- Tumours of the larynx - laryngeal papillomatosis

Based on location of obstruction

Supraglottic conditions

- Epiglottitis
- Retropharyngeal/lateral pharyngeal Abscess
- Retrotonsillar Abscess
- Peritonsillar Abscess
- Severe pharyngotonsillitis ± adenoiditis
- Faucial diphtheria

Subglottic conditions

- Viral croup
- Spasmodic croup
- Bacterial Tracheitis
- Angioneurotic oedema

Epidemiologic Risk Factors

- Age: 3months – 5years for subglottic lesions; 3 – 7 years for supraglottic lesions
- Sex: Male predilection
- Climate: Common in cold weather
- Aetiologic Agent: Viral -Subglottic; Bacterial-Supraglottic
- Endogenous Factor: Atopy
- Anatomic Defect

Pathogenesis and Pathophysiology

Upper Respiratory Tract Infection

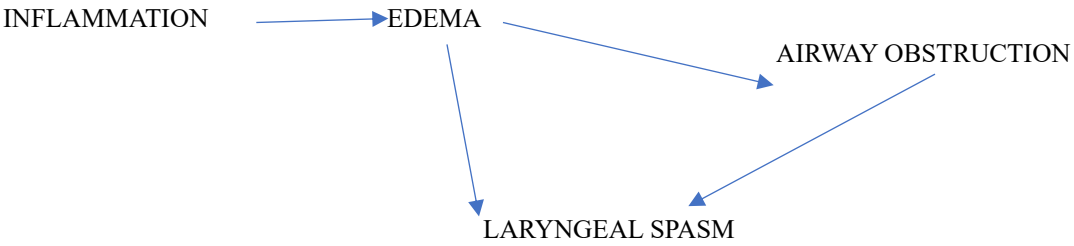

Figure 3: Pathogenesis and Pathophysiology of Upper airway Obstruction

Aetiologic Causes (Infectious)

Supraglottic

Bacteria – *H. Influenzae*

Subglottic

Viral – Parainfluenza virus 75%
- Adenovirus
- RSV
- Measles virus

Other Agents

-*Streptococcus pyogenes*

-*Streptococcus pneumoniae*

-*Staphylococcus aureus*

Inhalational Injury

-Acute airway compromise may occur following burns injury and associated oedema.

-Factors indicating potential inhalational injury include:

- High index when the burns involve the face and neck.
- History of exposure to smoke in a confined space

Foreign Body Aspiration

- Peak incidence: 1-2 years old
- Reasons:
- Lack of molars for effective chewing
- Play while eating
- Explore with mouths, unable to distinguish edible vs. inedible objects
- Location of lodged objects:
- Most in distal airway
- Occasionally in larynx or trachea
- Risk of complete airway obstruction

Trauma

- The airway may be compromised due to oedema or blood from traumatic causes.
- Trauma may be accidental or iatrogenic (post-intubation)
- Multiple attempts at intubation in infants could result in the rapid development of airway oedema

Anaphylaxis

-Anaphylaxis may develop over minutes and may cause potentially life-threatening airway, respiratory and circulatory compromise.

-Various triggers have been identified:

- Foods e.g. nuts, milk, seafood
- Venoms
- Drugs

Conclusion

-Paediatric acute upper airway obstruction is a critical condition requiring prompt recognition and intervention due to its potentially life-threatening nature.

-Understanding the anatomical and physiological differences in children's airways, as well as the various causes and risk factors for obstruction, is crucial for effective management and treatment.

-Key takeaways are:

- Children have smaller airways and a less mature immune system, making them more susceptible to obstruction from infections, allergies, and anatomical abnormalities.
- Upper airway obstructions can be congenital or acquired, with causes ranging from infections to trauma and foreign body aspiration.
- Inflammatory processes and the dynamic nature of the paediatric airway contribute to increased resistance and potential airway collapse, emphasizing the importance of early and accurate diagnosis.

Questions

1. Signs of a sudden severe upper airway obstruction include all of the following, EXCEPT:

a. Inability to speak.
b. Grasping the throat.
c. Acute cyanosis.
d. Forceful coughing.

2. The initial treatment to dislodge a severe foreign body airway obstruction in a responsive infant involves:

a. Blind finger sweeps.
b. Back slaps.
c. Abdominal thrusts.
d. Bag-valve mask ventilation.

3. A patient has been admitted to the ER. Which of the following symptoms indicate a diagnosis of angioedema?

a. 3 D's hallmark: dysphagia, drooling, distress.
b. Hoarse, breathy, raspy voice that may progress to breathing problems.
c. Asymmetric swelling of tongue and tachycardia.

d. Postnasal drip, nasal congestion, reduced sense of smell, breathing through mouth instead of nose.

4. Which maneuver elevates the head and extends the neck?
a. Sniffing position
b. Recovery position
c. Jaw thrust
d. Oropharyngeal airway

5. A newborn girl is transferred to the neonatal intensive care unit due to dyspnea and breath sounds consistent with upper airway obstruction. Her tongue is protruding from her mouth, but her mandible and other facial features are within normal limits. Her oxygen saturation is 89% on room air, which improves to 92% with jaw thrusting. She has not yet been intubated, and her airway appears to be protected with jaw thrust. What is the most appropriate next step in management?
a. Direct laryngoscopy and bronchoscopy.
b. Tongue-lip adhesion.
c. Emergent tracheostomy.
d. Racemic epinephrine.

6. A 3-year-old boy was brought to the emergency department by his mother after losing consciousness a few minutes ago. The mother tells the provider that her child was behaving normally 15 minutes ago when playing with his toys in his room. She left the room for a few minutes, and when she returned, he was crying, but his cry sounded abnormal. He lost consciousness on the way to the emergency department. What is the next best step in management?
a. Finger sweep of the mouth to clear foreign body.
b. Cricothyrotomy.
c. Emergent laryngoscopy.
d. Rapid sequence intubation.

KEYS

Question	1	2	3	4	5	6
Correct Answer	D	B	A	A	A	C

CLINICAL QUIZ

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

A 15-day old term male neonate weighing 3.7kg was referred from the immunisation clinic, on account of some abnormal movements and petechiae on the skin. The mother admitted the petechiae was noticed some seven days prior presentation and she also noticed very scanty bleed from the umbilical stump which she attributed to the dropping of the atretic umbilical stump on the day of presentation. The baby has stopped sucking of the breast and had some abnormal movements of the lower limbs. Laboratory investigations revealed a prolonged prothrombin time, platelet count of 220,000/μL and Packed Cell Volume (PCV) of 45%.
Figure 1 below shows the cranial CT of the baby.

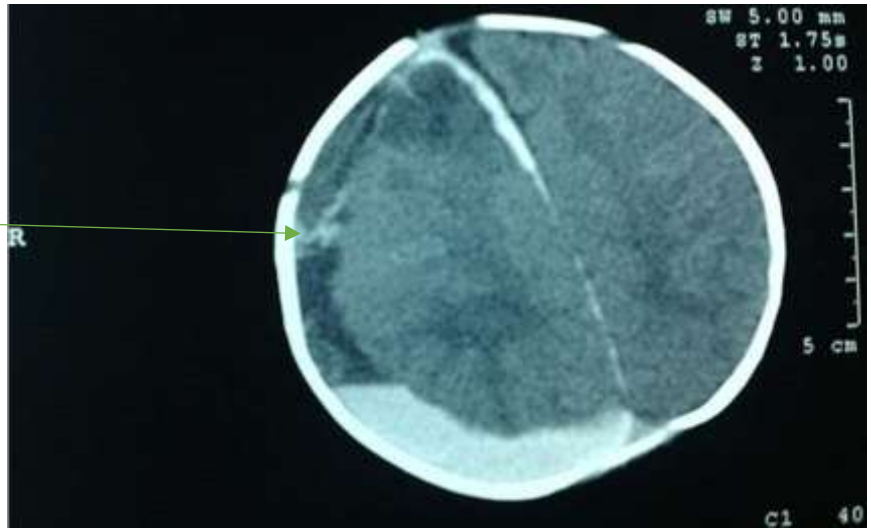

Figure 1: Representative Cranial CT scan.

Questions: Select the most appropriate answer to each question from the options A to D as provided.

1. Which of the following medical history is important and needs to be excluded in the mother?
a. Chronic alcohol consumption.
b. Chronic cigarette smoking.
c. Chronic Diabetic illness and use of antidiabetic agents.
d. Epilepsy and use of antiepileptic agents.

2. Which of the following medical history items supports the baby`s medical condition?
a. Administration of oral antibiotics to the baby prior petechiae onset.
b. Initiation of breastmilk substitute upon delivery of the baby.
c. Past medical history of early neonatal jaundice in the immediate elder male sibling.
d. Baby`s APGAR score of 7 and 10 at the first and fifth minutes of life.

3. Which of the following diagnosis best suits the baby`s medical condition?
a. Foetal Alcohol Syndrome.
b. Neonatal Hepatitis.
c. Neonatal Sepsis.
d. Haemorrhagic Disease of Newborn.

4. Which of the following investigations is the least important in further evaluation of the baby`s medical condition?
a. Blood film examination.
b. Bleeding time.
c. Clotting factors assay.

d. Fibrin degradation and Fibrinogen levels assay titres.

5. Which of the following laboratory findings is not expected of the baby`s medical condition?
a. Prolonged bleeding time.
b. Low Factor VIII level.
c. Low Fibrinogen level.
d. High Fibrin degradation assay titres.

6. Which of the following intervention is the most appropriate for the baby`s medical condition?
a. Intravenous antibiotics, administration of Vitamin K1, and follow-up immunisation.
b. Exchange blood transfusion with fresh whole blood, Intravenous antibiotics, administration of Vitamin K1, Craniotomy and follow-up immunisation with neuro-developmental surveillance.
c. Intravenous antibiotics, Intravenous administration of Vitamin $K_{1,}$ administration of fresh frozen plasma, Craniotomy and follow-up immunisation with neuro-developmental surveillance.
d. Administration of Vitamin K1, Intravenous antibiotics, Plasmapheresis and follow-up immunisation with neuro-developmental surveillance.

Answers to the questions with the relevant clinical explanations

Question 1: Correct answer - D

Chronic maternal use of drugs that interfere with Vitamin K functions like phenytoin and phenobarbitone are associated with the development of haemorrhagic disease of newborn (HDN), also known as Vitamin K deficiency bleeding (VKDB) which results from Vitamin K deficiency. Although HDN in the classical type, usually manifests within the first few days of life with more florid symptoms, it could also occur any day within the first few weeks of life. The first symptoms were apparently noticed on the eighth day of life with florid clinical manifestations later suggesting a severe form of the disease condition.

Question 2: Correct answer - A

The use of antibiotics in this baby could hamper the normal activity of the intestinal bacterial flora which is needed to produce natural Vitamin K. The good APGAR Scores of the baby precludes Perinatal Asphyxia which is a risk factor for HDN. There are no direct links between HDN and the other factors listed

Question 3: Correct answer - D

The baby's presentation is not in keeping with Foetal Alcohol Syndrome (FAS) which manifests with abnormal facial appearance, low birth weight, and delayed developments among others. The baby did not have any of the features of FAS as per his age. Similarly, there are no features suggestive of sepsis and hepatitis as the baby did not have jaundice, fever, or a positive history of maternal hepatitis. The baby`s clinical condition best suits the diagnosis of HDN. The baby manifested severe form of the disease by virtue of the right subdural hematoma identified on cranial CT scan.

Question 4: Correct answer - A

The diagnosis of HDN/ VKDB is mainly clinical and supported by laboratory findings. The condition results from Vitamin K deficiency and platelets are not involved in the pathogenesis of the disease hence, neither qualitative nor quantitative platelet abnormalities are expected. The normal platelet count affirms lack of quantitative platelet disorder. Although a peripheral blood film could allow for a qualitative study of the platelets, the lack of roles for the platelets in the diagnosis of HDN blunts the need for this examination. The bleeding time is usually normal in HDN but prolonged in disseminated intravascular coagulopathy (DIC) which is a differential diagnosis of severe HDN. Also, clotting factors assay is very important as only a few clotting factors are deficient in HDN (Factors II, VII, IX and X) as against DIC which is very consumptive and associated with several clotting factors deficiencies. In addition, DIC is associated with consumption/depletion of fibrinogen and accumulation of fibrin degradation products. These are not known to occur in HDN/VKDB.

Question 5: Correct answer - A

The bleeding time is not prolonged in HDN; similarly, Factor VIII level is usually normal. Furthermore, both the fibrinogen and fibrin degradation products levels

are normal in HDN. However, these are affected in DIC, a differential diagnosis of severe form of HDN.

Question 6: Correct answer - C

Intravenous administration of Vitamin K_1 (5 -10mg) daily, use of fresh frozen plasma and craniotomy to evacuate the right subdural haematoma with follow-up immunisation and neuro-developmental surveillance are the most appropriate interventions for this baby. Although exchange blood transfusion with fresh whole blood could serve as a source of some of the deficient clotting factors for the baby, the yield of the deficient clotting factors will be small and inadequate to meet the needs of the baby when transfused with whole blood hence, the need for the use of fresh frozen plasma at the rate 10mls/Kg alongside intravenous Vitamin K_1 is preferred in severe HDN/VKDB. The fresh frozen plasma will supply the deficient clotting factors. The index case has a severe form of HDN that requires the use of both fresh frozen plasma and intravenous Vitamin K_1. The use of the oral or intramuscular routes for Vitamin K administration is not encouraged. It could be inefficient in the case of oral route administration given the florid manifestations of HDN in this baby and intramuscular administration could also provoke intramuscular bleeding. The baby neither had features suggestive of anaemia nor sepsis to warrant exposure to the several risks associated with exchange blood transfusion. Plasmapheresis is not relevant in this case as there are no unwarranted antibodies that must be removed. It is important to stress that the baby must be vaccinated according to the National Guidelines at the immunisation clinic follow-up visits to prevent missed opportunity for immunisation. Neuro-developmental surveillance is very important to monitor the child for any sequala following the intracranial bleeding that he suffered.

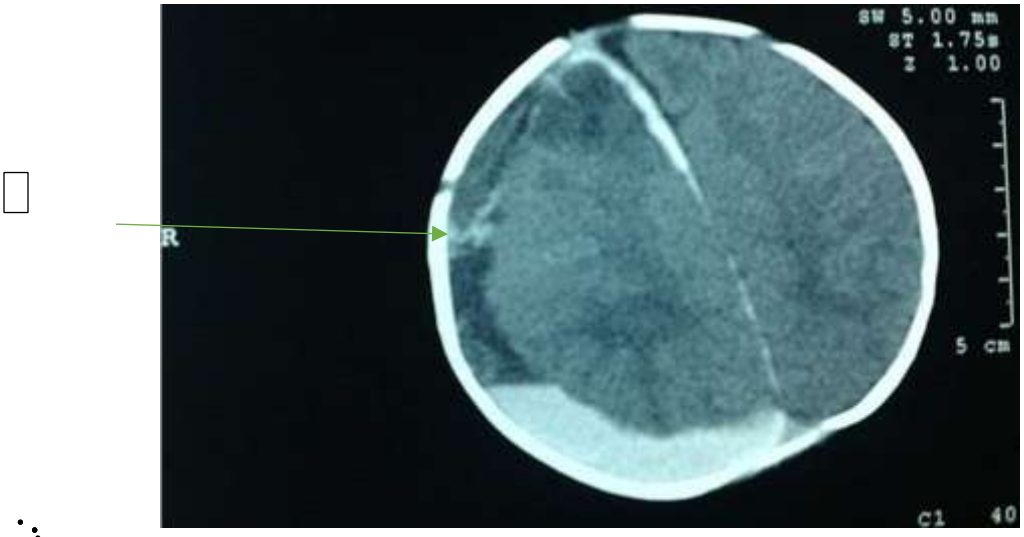

Figure 1: Computerised tomographic brain scan showing a large right subdural haematoma

Adapted from: Boujan MM, Sharef KH. Change in hospital protocol regarding the use of vitamin K prophylaxis in newborns following a case of spontaneous subdural haematoma in a previously healthy 40-day-old infant. East Mediterr Health J. 2013 May;19(5):502-5.

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