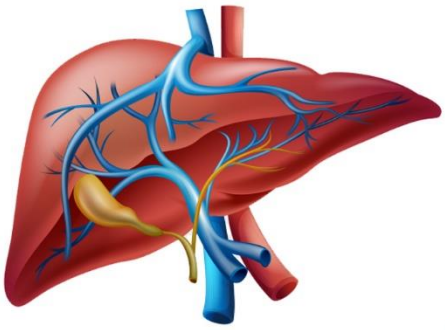
Pediatric Hepatology Protocol of EHA



First Edition 2024

Egyptian Clinical Practice Protocols

in

Pediatric Hepatology

for

Egypt Healthcare Authority

First Edition

2024

Prepared by

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Egyptian Clinical Practice Protocols

in

Pediatric Hepatology

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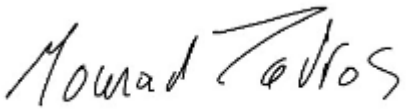

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PREFACE

Recently, there is an increasing need to provide programs with accurate competency-based assessments to ensure the delivery of high-quality healthcare. The aim of developing these Egyptian Clinical Practice Protocols in Pediatric Hepatology is to unify and standardize the delivery of health care to all pediatric patients with liver diseases at all heath facilities.

The Egyptian Clinical Practice Protocols in Pediatric Hepatology are developed to enable health care providers, especially on the primary care level, to apply stepwise diagnosis and management of pediatric liver diseases/disorders. By applying these protocols, healthcare providers will be able to **(a)** recognize common clinical presentations of pediatric liver disease/disorders, **(b)** identify and implement emergency interventions required for urgent cases (e.g., upper gastrointestinal bleeding), **(c)** pinpoint the cases that need urgent referral to secondary and tertiary care without delay (e.g., biliary atresia cases) and **(d)** distinguish neonatal jaundice secondary to hepatic disease (direct hyperbilirubinemia) from the huge volume of newborns with physiological jaundice and direct them to proper medical care.

These Egyptian Clinical Practice Protocols in Pediatric Hepatology are dynamic tools, reflecting the current state of literature and practice, in the field of Pediatric Hepatology, at the time they were produced and are amenable to periodic revisions. Most of the content herein is based on the most recent literature, including the latest Practice Protocols produced by respectable societies in the field of Pediatric Hepatology: European, North American and British Societies of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN, NASPGHAN, BSPGHAN). All flowcharts/algorithms were produced with 100% agreement of all members of the Working Group for Development of Egyptian Clinical Practice Protocols in Pediatric Hepatology for Egypt healthcare authority.

As a start, four subjects were agreed upon to be developed in the form of flowcharts/algorithms for diagnosis and management including: direct hyperbilirubinemia in neonates and infants, acute hepatitis, chronic liver diseases and upper gastrointestinal bleeding in the pediatric age group.

Knowing the large number of patients, the practitioner can face, and the importance of initial management of children with hepatic diseases using a clear strategy, these protocols were meticulously and scientifically prepared in order to provide proper and sound management, saving time and resources. Each algorithm contains a stepwise approach according to the level of medical care. It was with 100% agreement of all members that the protocols were developed using color coding: green for primary care, yellow for secondary care and red for tertiary care. For more details about each algorithm, the users are asked to refer to the matched-numbered text on the corresponding page.

These Egyptian Clinical Practice Protocols in Pediatric Hepatology were produced by the joint efforts of a group of consultants in Pediatrics, Pediatric Hepatology, Epidemiology and Egypt healthcare authority. The working group was initially divided in 4 subgroups each working on one of the chosen subjects, followed by an extended discussion of each subject attended by all members until the final version was approved. All these efforts were offered voluntarily extending over a period of three months of meticulous work, including over thirty hours of online meetings for discussions by all group members.

Expected tasks post-production of these Egyptian Clinical Practice protocols in Pediatric Hepatology include: (a) training of primary care physicians to use these protocols, (b) evaluation of the feedback from end users, both physicians and patients, (c) revision of the protocols on annual basis and (d) establishment of an accurate database of liver diseases in the pediatric population and registry of various diseases on a national level.

Ultimately, we hope that, soon enough, health authorities will be convinced with the increasing needs for including pediatric patients with rare liver diseases under the umbrella of Egypt healthcare authority, as they cumulatively constitute a considerable health problem.

Members of the Working Group

For Development of the Egyptian Clinical Practice Protocols

In Pediatric Hepatology

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List of Abbreviations

ABG	*Arterial Blood Gases*
ALT	*Alanine Aminotransferase*
ALP	*Alkaline Phosphatase*
ANA	*Antinuclear Antibodies*
AST	*Aspartate Aminotransferase*
BA	*Biliary Atresia*
BASM	*Biliary Atresia Splenic Malformation*
BP	*Blood Pressure*
CBC	*Complete Blood Count*
CBD	*Common Bile Duct*
CMV	*Cytomegalovirus*
CPK	*Creatine Phosphokinase*
DNA	*Deoxyribonucleic Acid*
EBV	*Epstein-Barr Virus*
ERCP	*Endoscopic Retrograde Cholangiopancreatography*
EUS	*Endoscopic Ultrasonography*

fT4	*Thyroxine*
GCS	*Glasgow Coma Scale*
GGT	*Gamma Glutamyl Transferase*
HAV	*Hepatitis A Virus*
HAV IgM	*Hepatitis A Virus Immunoglobulin M*
Hb	*Hemoglobin*
HBcAb	*Hepatitis B Core Antibody*
HBsAg	*Hepatitis B Surface Antigen*
HCVAb	*Hepatitis C Virus Antibody*
HCV RNA	*Hepatitis C Virus Ribonucleic Acid*
IG	*Immunoglobulin*
IgG	*Immunoglobulin G*
IM	*Intramuscular*
INR	*International Normalized Ratio*
IV	*Intravenous*
LFT	*Liver Function Tests*
LKMA	*Liver-Kidney Microsomal Antibodies*
NAFLD	*Non-Alcoholic Fatty Liver Disease*

MRCP	***Magnetic Resonance Cholangiopancreatography***
NICU	***Neonatal Intensive Care Unit***
NPO	***Nothing Per Oral***
p-ANCA	***Perinuclear Antineutrophil Cytoplasmic Antibody***
PCR	***Polymerase Chain Reaction***
PPI	***Proton Pump Inhibitors***
PT	***Prothrombin Time***
PTT	***Partial Thromboplastin Time***
RBCs	***Red Blood Cells***
RBS	***Random Blood Sugar***
RR	***Respiratory Rate***
SMA	***Smooth Muscle Antibodies***
TSH	***Thyroid Stimulating Hormone***
tTG	***Tissue Transglutaminase***
UTI	***Urinary Tract Infection***

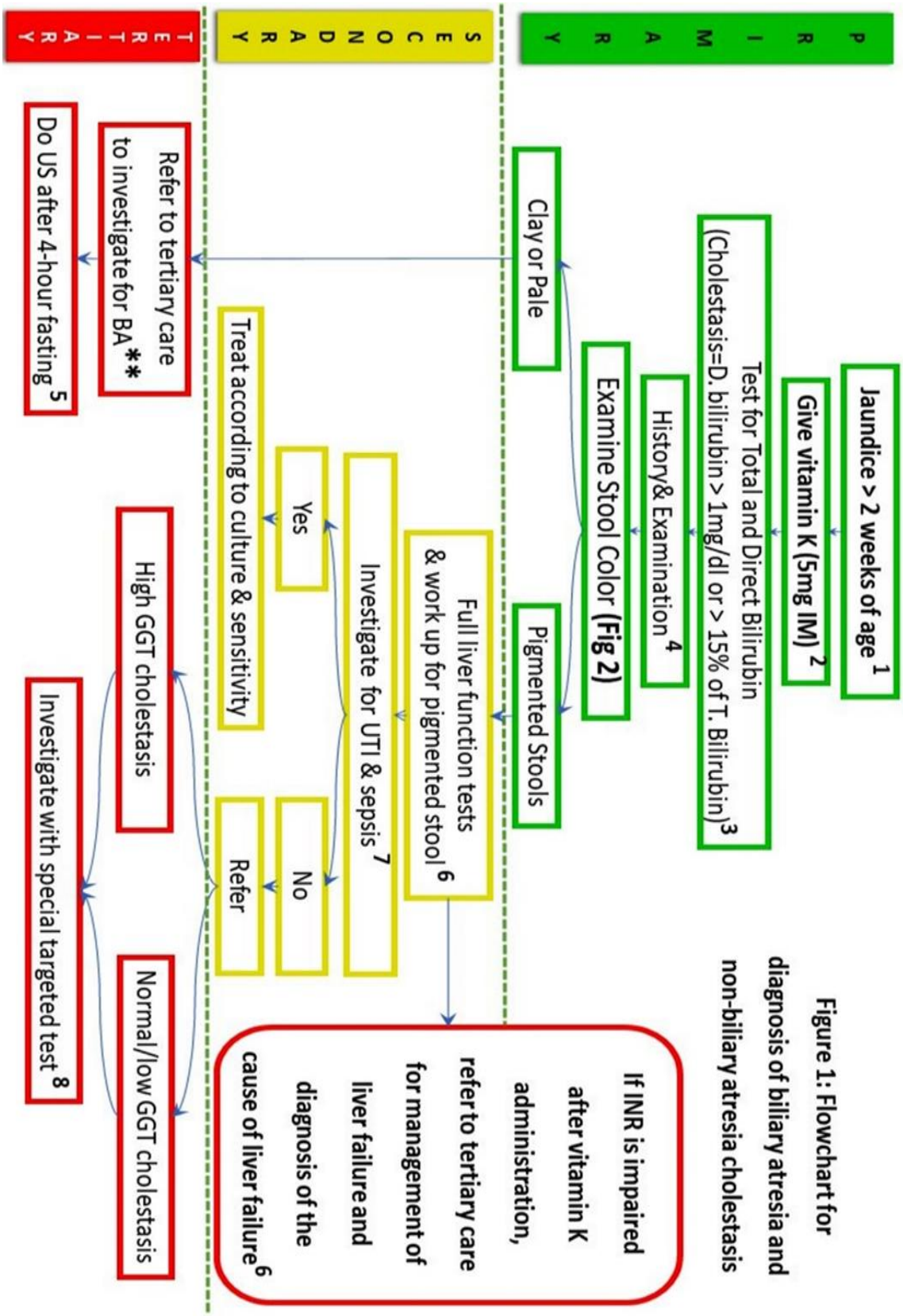

Figure 1: Flowchart for diagnosis of biliary atresia and non-biliary atresia cholestasis

Figure (1): Flow chart diagnosis of biliary atresia & non-biliary cholestasis

Key Points in Neonatal Cholestasis

1- All Infants Who Are Jaundiced:

- At 14 days of life (> 37 weeks gestation or artificially fed babies), or
- At 21 days (< 37 weeks gestation or breastfed babies), or
- Any newborn from day1 with jaundice, dark colored urine, and/or pale stools

Should be promptly investigated for conjugated hyperbilirubinemia

2- Vitamin K (5 mg IM):

- Should be given to all cholestatic babies to correct coagulopathy and prevent bleeding (most serious is intracranial hemorrhage).

3- Conjugated Hyperbilirubinemia

- Is defined as a direct (conjugated) serum bilirubin level > 1 mg/dl or > 15% of total serum bilirubin.

4- History & Examination:

- Onset of jaundice, NICU admission, medications received, parenteral nutrition, results of newborn screening tests
- Prenatal history: maternal infections, medication, maternal illness
- Family history: consanguinity, similar condition in siblings or family
- Color of urine (deep yellow). Examine the diaper for urine color (colorless in healthy newborn)
- Color of stools (using Stool Color Cards: Figure 2). Examine the stool color yourself.
- Pale stools to investigate for biliary atresia (BA)
- Pale/sick appearance: lethargy, irritability (infections or metabolic disease)
- Failure to thrive, small for gestational age (congenital infections, metabolic diseases)

NB: Infants with BA typically appear well with adequate growth at presentation.

- Dysmorphic features, eye and hearing abnormalities (Alagille syndrome, metabolic disease, congenital infections)
- Cardiac anomalies: congenital infections, BASM syndrome, Alagille syndrome
- Abdominal examination: Firm hepatomegaly is suspicious of BA; hepatosplenomegaly may be present in storage or hemolytic diseases.
- Hypoplastic male genitalia may be present in panhypopituitarism.

5- Imaging: Fasting abdominal ultrasound:

- To detect surgical causes of cholestatic jaundice (BA, choledochal cyst), assess liver size and echogenicity, splenic size, ascites, renal size and echogenicity, patency of portal and hepatic vessels.

NB: HIDA scan is not specific and can hardly distinguish BA from other causes of cholestatic jaundice. It is NOT recommended in the workup of neonatal cholestasis.

6- Laboratory test:

- Liver Function Tests (LFT): total and direct serum bilirubin, ALT, AST, ALP, GGT, serum albumin, PT, INR, should all be done simultaneously. LFT may point to some etiologies (normal GGT cholestasis) however, they are non-specific.
- If INR is still impaired after vitamin K administration: Refer to Tertiary care for diagnosis and management of liver cell failure.
- Complete blood count: look for cytopenias.
- Blood & urine cultures
- DO NOT TEST for viral hepatitis A, B, and C markers unless there is a clear history of exposure.
- RBS: Hypoglycemia should be prevented by adequate feeding or iv fluids in critically ill.

7- Treat neonatal sepsis or UTI by appropriate antibiotics.

8- Special targeted tests according to suspected etiologies to be discussed with Pediatric Hepatologist:

- TSH, FT4, early morning cortisol level
- Serum ammonia and lactate
- TORCH screening especially CMV DNA by PCR
- Reducing substances in urine and galactose-1-P-uridyl transferase
- Succinyl acetone in urine or blood
- Tandem mass spectrometry
- Plasma and urine organic acids
- Serum bile acids
- Sweat chloride test
- Echocardiography for cardiac anomalies
- Spine X-ray for vertebral anomalies
- Fundus and/or slit lamp examination
- Liver biopsy
- Genetic testing: targeted gene panels, whole exome sequencing.

Biliary Atresia

- BA is the most common cause of cholestatic jaundice affecting up to 40% of infants.
- It is crucial to diagnose BA early enough for optimal management.
- Initial good general condition and proper weight gain of these infants is certainly **MISLEADING** and leads to late diagnosis and referral to specialized centers.
- LFT **are non-specific**.
- **Fasting (for 4 hours) abdominal ultrasound** will help identify BA:
  - Absent, atrophic, irregular morphology gall bladder,
  - Abdominal heterotaxy (situs inversus, meso-position of liver),
  - Polysplenia. asplenia
- **Liver biopsy** is the mainstay for diagnosis with an accuracy of up to 90%.
    - Histopathological characteristics confirming BA include:
      - Bile duct proliferation,
      - Portal fibrosis and edema,
      - Bile plugs formation,
      - Absence of sinusoidal fibrosis.

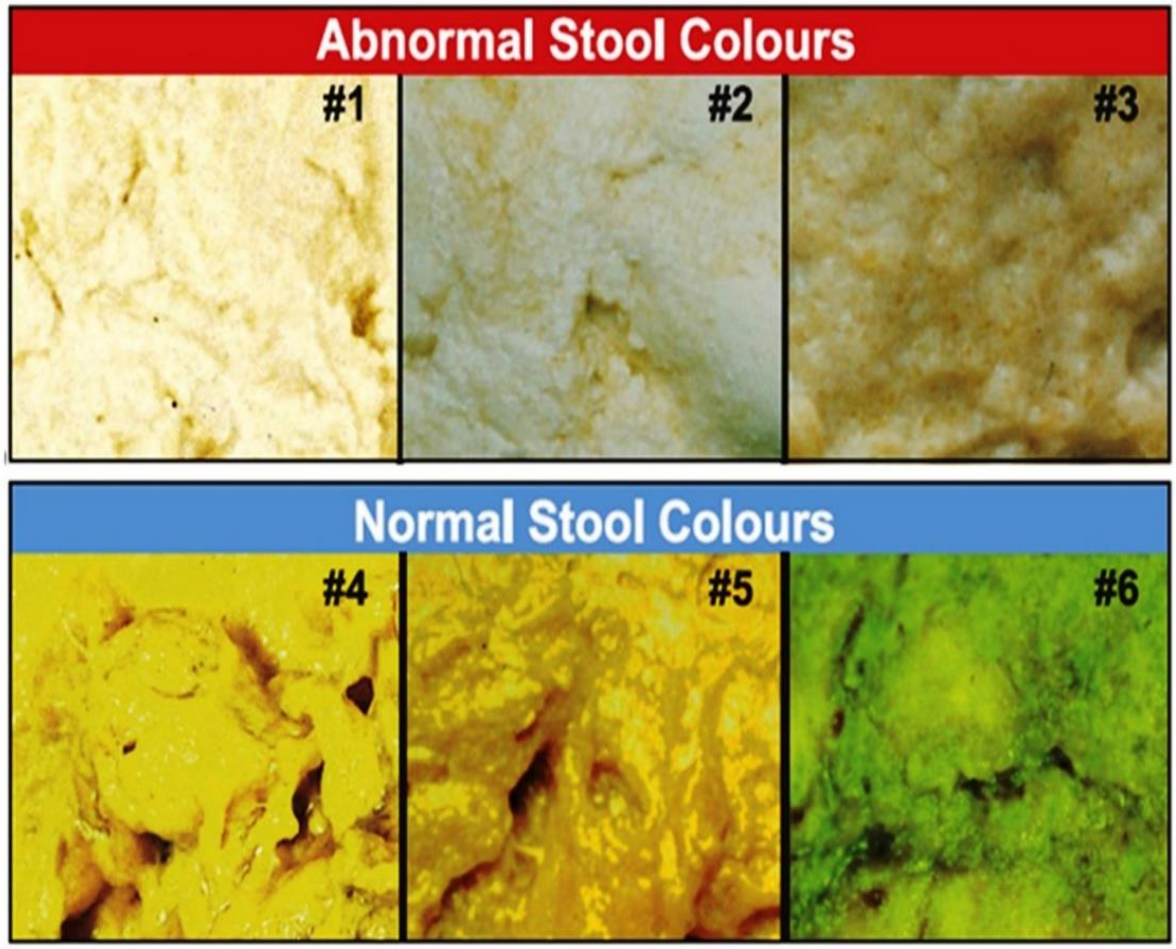

Figure 2: Stool Color Card

(Chen S-M, Chang M-H, Du J-C, Lin C-C, Chen A-C, Lee H-C, Lau B-H, Yang Y-J, Wu T-C, Chu C-H, Lai M-W, Chen H-L. Screening for biliary atresia by infant stool color card in Taiwan. Pediatrics 2006; 117: 1147-54.)

Figure (2): Stool color cards

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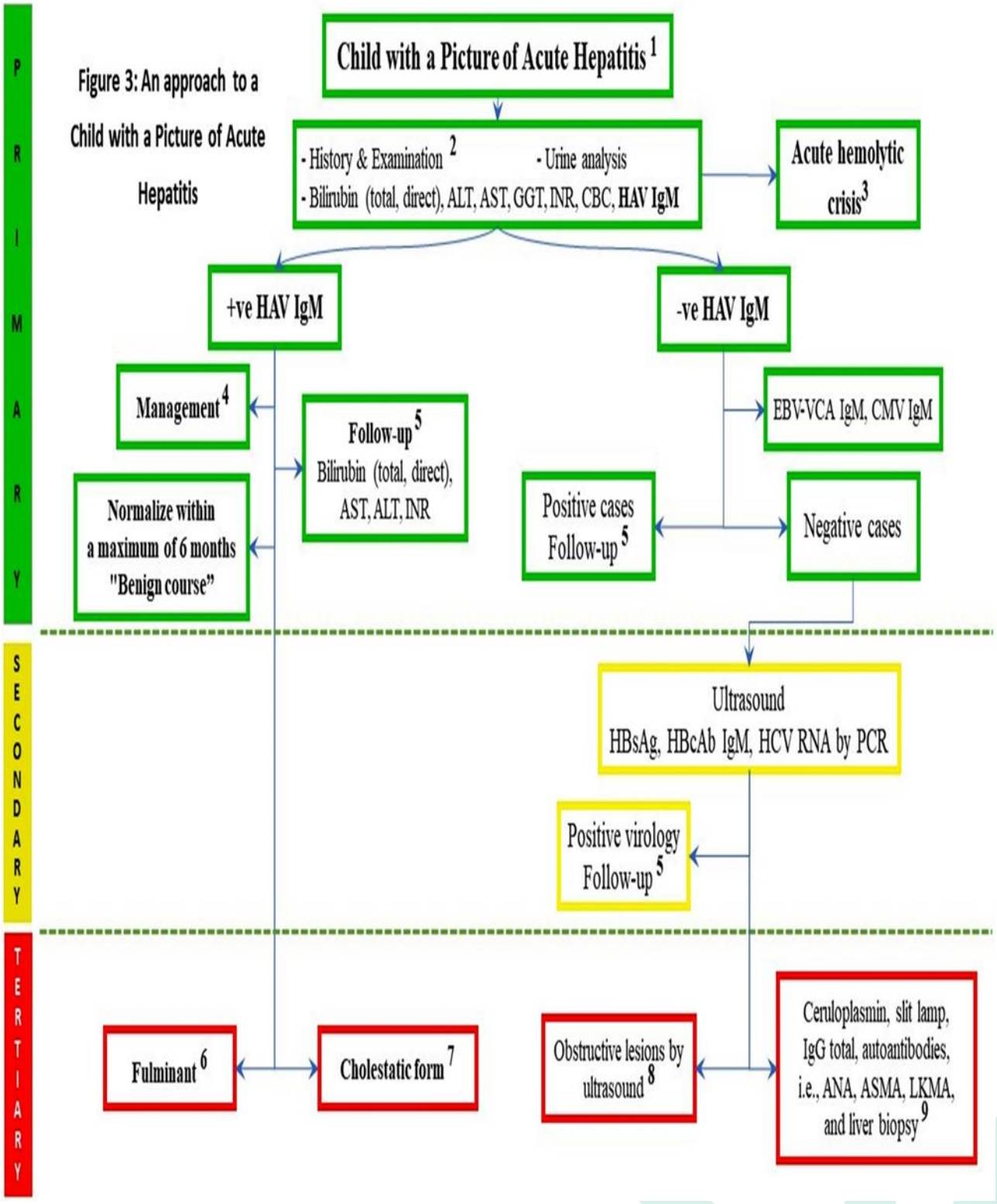

Figure (3): An approach to a child with a picture of acute hepatitis

Child with a Picture of Acute Hepatitis

1. *Picture of Acute Hepatitis:*

- Acute onset of jaundice, dark urine and pale stools for <15-day duration.

2. *History:*

- Acute hepatitis is usually preceded by history of prodromal symptoms for few days, i.e., anorexia, nausea, malaise, diarrhea, vomiting and fever. History of contact to a jaundiced case or drug intake. Examination: mild to moderate tender hepatomegaly, and occasionally splenomegaly and elevated ALT >100 IU/mL.

N.B:

- The degree of elevation of transaminases does not correlate with the severity of the illness.
- Rarely patient may present with extrahepatic manifestations accompanying the acute illness, e.g., hydrops of the gall bladder (acalculous cholecystitis), autoimmune hemolytic anemia, aplastic anemia, acute reactive arthritis, or acute pancreatitis. Refer to a tertiary hospital.

3. *Acute Hemolytic Crisis:*

- **Manifested by acute onset of jaundice, with the following criteria:**
  - Hemoglobin in urine
  - Anemia
  - Indirect hyperbilirubinemia with normal ALT.

"Refer to a secondary hospital for evaluation and possible blood transfusion"

4. Management of HAV Infection is Mainly Supportive:

Do	Do Not
✓ Advise rest according to child tolerance.	☒ Restrict protein.
✓ Adequate hydration.	☒ Add extra sugar or carbohydrates
✓ Nutritional support: balanced diet.	
✓ Antiemetic (Ondansetron) and antipyretic (Paracetamol within the recommended daily doses).	☒ Give herbal remedies
✓ Proper hand hygiene of cases and caregivers	
✓ Bathroom hygiene: disinfect, using house bleach, all objects touched by hands.	☒ Give vitamins unless indicated.
✓ Absence from child care or school: for at least 1 week of onset of symptoms if the child is toilet trained, 2 weeks if not trained or having diarrhea and > 2 weeks if the child general condition is not back to normal.	

How to prevent transmission of infection among household members?

- **Post-exposure immune prophylaxis within 14 days of exposure:**
  - Active immunization with HAV vaccine for those above 12 months of age.
  - Passive immunization using immunoglobulin: in a dose of 0.1 mL/kg IM for infants younger than 12 months old, and in whom vaccine is contraindicated.
  - HAV vaccine and immunoglobulin: in immunocompromised, and those with chronic liver disease.

5. Follow-up:

- Clinical assessment and investigations biweekly in the first month then, monthly till normalization. If no normalization till 6 months refer to tertiary care. If confirmed acute HBV or HCV refer to tertiary care even after normalization of ALT.

6. Fulminant Hepatic Failure:

- INR ≥1.5 not corrected by vitamin K in the presence of clinical encephalopathy or INR ≥ 2.0 regardless of the presence or absence of clinical encephalopathy. Give IV/IM vitamin K before referral for hospitalization.

7. Cholestatic Form:

- Pruritus, pale stools, fatigue, and weight loss.

8. Obstructive Lesions:

- By ultrasound including common bile duct stone, choledochal cyst.

9. Investigations for Chronic Diseases:

- Presented by acute hepatitis as autoimmune hepatitis or Wilson disease (Refer to chapter on chronic liver disease).

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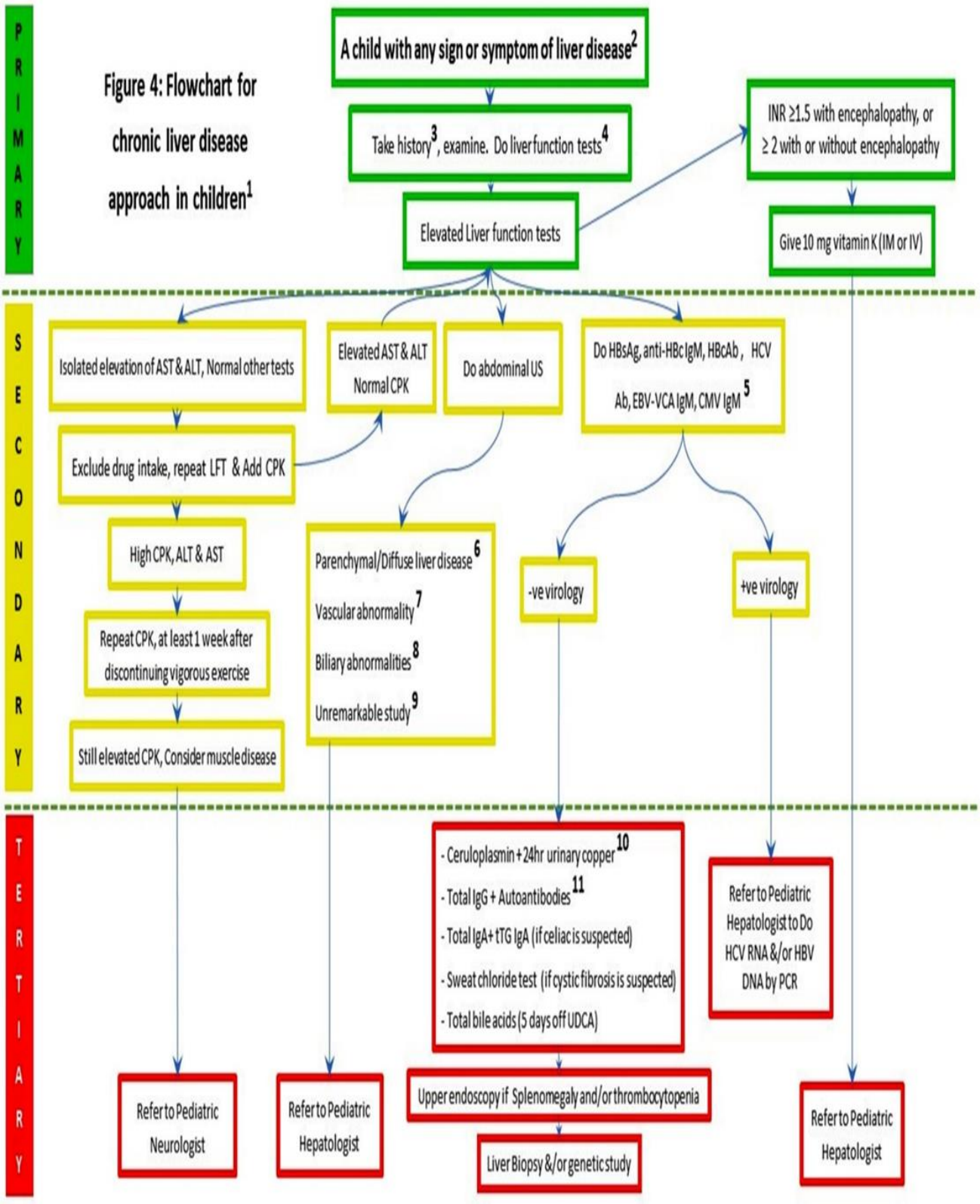

Figure (4): Flowchart for chronic liver disease in Children

Key points in Chronic Liver Disease in Pediatrics

1. *Definition:*

Chronic liver disease is defined as ongoing liver injury for at least 6 months. However, it is unwise to wait for 6 months before investigating a possible cause of liver damage, as some hepatopathies, such as autoimmune liver disease or Wilson's disease, can become rapidly life-threatening without appropriate treatment.

2. Clinical Presentations (Signs and Symptoms):

- Jaundice and/or hepatomegaly, hepatosplenomegaly, splenomegaly, ascites.
- Associated symptoms may include bleeding tendency, lower limb edema, pruritus, and disturbed conscious level.
- Non-specific clinical symptoms may include anorexia, fatigue, nausea, vomiting, or abdominal pain.
- Hematemesis secondary to variceal bleeding may be the first symptom in a child with chronic liver disease or with portal vein thrombosis.
- Faltering growth/growth failure, with weight and height percentiles below the average for age or muscle wasting indicates chronic liver disease early in life. Presence of ascites and organomegaly may mask decreased weight percentiles.
- A child with chronic liver disease may be asymptomatic with only incidental finding of elevated transaminases.
- The presence of doll facies, increased appetite, night sweating, and or convulsions may suggest the possibility of glycogen storage disease.
- Overweight/obesity with high BMI in an older child may suggest the possibility of nonalcoholic fatty liver disease.

3. History Taking:

Ask About:

- Consanguinity, draw a family pedigree. Ask about family history of chronic liver disease. Family history of auto immune disorders like SLE may suggest the possibility of autoimmune hepatitis.
- Risk factor of viral hepatitis like history of blood transfusion or operations.
- Drug intake, such as antiepileptics, and non-steroidal anti-inflammatory drugs.
- Family history of gall bladder stones, cholestasis of pregnancy, or history of cholestasis of infancy that resolved or improved partially that may suggest the possibility of PFIC3.
- Cardiac symptoms suggestive of right sided heart failure with congestive hepatomegaly.
- Poorly controlled type 1 diabetes mellitus for the possibility of glycogenic hepatopathy.

Pitfalls in the Diagnosis of Chronic Liver Disease:

- **Splenomegaly with non-palpable liver is met with in cases of:**
  - ✓ Liver cirrhosis in which there is shrunken liver associated with portal hypertension.

OR

  - ✓ Portal vein thrombosis in which there is pre-hepatic portal hypertension with normal liver size and normal liver function tests.

- **Do not miss to palpate the left lobe of the liver, in case of cirrhotic shrunken liver, left lobe is felt firm in mid line. If normal liver as in case of portal vein obstruction, left lobe is soft, not felt and even only detected by light percussion.**
- **Don't miss percussion of the upper border of the liver, to assess the liver size (to exclude ptosed liver).**

4. Interpretation of Liver Function Tests:

- **8 Tests to be done at the same setting:**

A.*Total and direct serum bilirubin:*

- Test for secretory functions of the liver. Only conjugated (direct) bilirubin passes in urine. Dark urine or urine analysis positive for bilirubin indicates direct hyperbilirubinemia.

B.*AST and ALT: detect liver injury.*

- Although elevated AST&ALT reflect hepatocyte injury, they do not always reflect the degree of liver injury.
- Isolated elevation of AST &ALT within a completely normal panel of liver functions may indicate muscle origin. Assess for Gower sign and pseudohypertrophy of calf muscles & ask for CPK.
- Difficult sampling may cause some rise of AST.

C.*GGT and ALP: detect impaired bile flow or biliary dysfunction.*

- GGT is not produced from bone tissue, so it confirms the hepatic origin of raised ALP in a growing child.
- Reference for GGT is age related, with higher levels in neonates (up to 385 IU/L), to reach less than 75 IU/L in 4 months of age.

D.*Albumin and PT &INR: test the synthetic functions of the liver.*

- In decompensated chronic liver disease, abnormal hepatic synthetic function is denoted by hypoalbuminemia and a prolonged prothrombin time & international normalized ratio (INR)
- High INR may reflect vitamin K deficiency. Administer vitamin K and assess the response on the next day. Prolonged INR after vitamin K (10 mg IM or IV) administration indicates significant hepatic dysfunction, either acute or chronic.

E.*Serum ammonia:*

- Test the detoxifying function if liver cell failure is suspected.

5. Viral Markers:

- ***HBsAg:***

  Indicates chronic hepatitis B infection, associated with positive anti HBc.

- ***Anti HBc (isolated):***

  Indicates exposure to HBV infection.

- ***Anti HBc IgM:***

  Is positive in acute HBV infection and with reactivation.

- ***HCV Ab (isolated):***

  Indicates previous exposure to HCV.

- ***HCV RNA:***

  Indicates active infection.

- ***Anti EBV VCA IgM &Anti CMV IgM:***

  Are performed if the disease duration is less than 6 months.

6. Parenchymal /Diffuse Liver Disease:

- ***Bright liver by US:*** mostly excess glycogen or fat**.**
  - Glycogen storage disease is suggested if bright liver is associated with short stature, doll like facies, hypotonia with delayed motor milestones. Check for hypoglycemia in the form irritability, excessive sweating or convulsions.
  - In an older child with BMI ≥85th percentile, consider NAFLD. In absence of red flag signs (chronic fatigue, GI bleeding, jaundice, splenomegaly, firm liver on examination, enlarged left lobe of the liver, low platelets, low white blood cell count, elevated direct bilirubin, prolonged INR, long history of elevated liver enzymes >2 years), council for diet and exercise. Repeat liver functions after 10% reduction of body weight.
  - If positive red flag signs from the start OR persistent raised transaminases after weight reduction REFER to pediatric hepatologist for further testing.
  - **Bright liver with normal BMI:** Do TSH & freeT4 and check for HbA1C, if normal, REFER to pediatric hepatologist for lysosomal acid lipase (LAL) in leucocytes or cultured fibroblasts/or genetic study for diagnosis of cholesteryl ester storage disease.

7. Vascular Abnormality by US:

- If portal vein thrombosis or attenuated hepatic veins (Budd Chiari disease), test for thrombophilia
- If congested hepatic veins, check neck veins and do echocardiography to exclude right sided heart failure and pericardial disease then REFER to cardiologist.
- Further studies including Doppler study, Triphasic CT and/or CT angiography may be needed.

8. Biliary Abnormalities:

- For gall bladder stones, do hemolytic profile & lipid profile & REFER to pediatric hepatologist to assess need for surgery.
- Choledochal cyst REFER to pediatric surgery.
- Intrahepatic biliary radicles dilation is suggestive of Caroli disease.
- CBD dilation may be due to CBD stricture, stone or pancreatic mass.
- In cases with intrahepatic biliary radicles, CBD dilation or choledochal cyst further investigations may include MRCP &/or ERCP (therapeutic) or EUS (especially for pancreatic lesions).

9. Unremarkable US Findings:

- In a child with chronic liver disease ultrasonography may appear normal.

10. Wilson Disease:

- Diagnostic tests include: low serum ceruloplasmin <20 mg/dl, 24-hr urine copper excretion >40 µg/24hrs, Kayser-Fleischer rings by slit-lamp examination (by a skilled ophthalmologist), molecular testing (for common mutation or whole exome sequencing) or liver biopsy for copper content (>250µg/g dry weight).

11. Autoimmune Hepatitis:

- Is diagnosed after exclusion of other causes of chronic liver disease in presence of high immunoglobulin G together with positive autoantibodies (ANA and/or SMA [titre≥1/20] in type1, anti LKM-1 [titre≥1/10] in type 2). Positive p-ANCA is detected in type 1 when associated with sclerosing cholangitis. Liver biopsy shows piece meal necrosis/interface hepatitis.

Infants Born to HBV or HCV Positive Mothers

Infants Born to HBsAg +ve Mothers:

- Should receive 0.5 cc of HBIG IM within 12 hours of birth (and maximum within 48 hours), in addition to zero dose of hepatitis B vaccine in a separate thigh. Then continue the regular vaccination schedule.

Asymptomatic Infants Born to HCV +ve Mothers:

- Can be screened for HCV using HCV Ab after 18 months of age. If positive, wait till age of available treatment (3 years) BUT don't forget to teach the family about precautions to prevent horizontal transmission within the family. At 3 years of age, ask for quantitative HCV RNA by PCR and refer for treatment if positive.

Mothers Positive for Either HBV or HCV:

- Should be encouraged to breast feed.

Any Case with HBV or HCV, Family Screening is Mandatory

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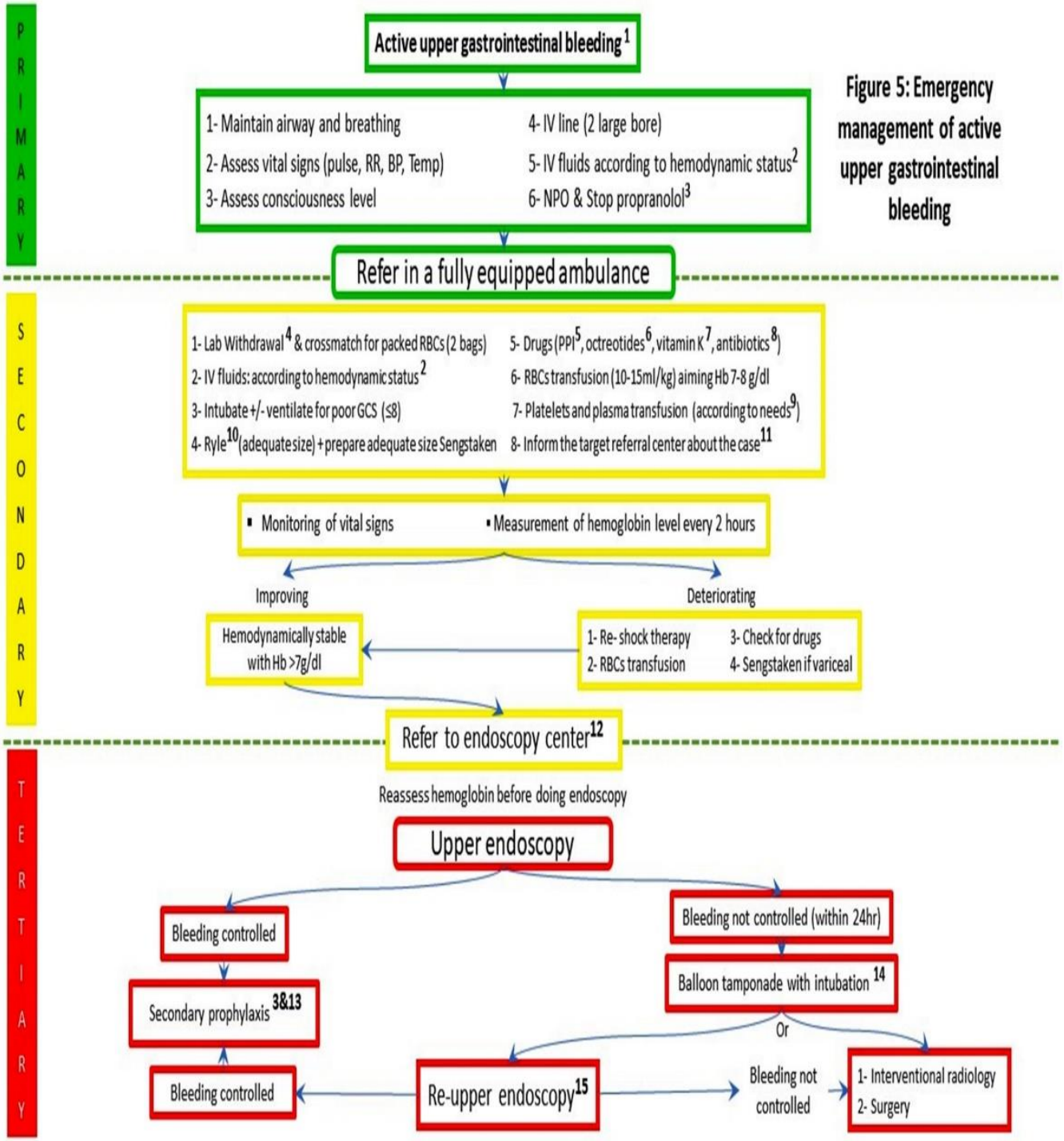

Figure 5: Emergency management of active upper gastrointestinal bleeding

Figure (5): Emergency management of active upper gastrointestinal bleeding

Key Points in Upper Gastrointestinal Bleeding

1. Active UGIB:

- Is defined as either hematemesis, coffee-ground vomitus, melena, or bleeding per rectum with hemodynamic instability.

2. IV Fluids:

- Should be given according to hemodynamic status; shock, deficit, or maintenance.

Symptoms of Hypovolemic Shock:

Tachycardia, Tachypnea, Hypotension, changed state of consciousness (irritability, confusion, unconsciousness), cool clammy skin, and low urine output.

Shock Therapy:

20 ml/kg normal saline 0.9% and could be repeated up to 3 times till the patient is hemodynamically stable.

Maintenance Fluids:

Give 2/3 of calculated maintenance IV fluids. Maintenance fluid calculation; first 10 kg of body weight: 100 ml/kg. Second 10 kg of body weight: 50 ml/kg. Third 10 kg of body weight and more: 25 ml/kg.

3. Propranolol:

- Stop propranolol during active bleeding if the patient was maintained on it.

4. Lab:

- ABG, RBS, CBC, kidney function (urea and creatinine), liver function tests (total and direct bilirubin, total protein, albumin, ALT, AST, ALP, GGT), electrolytes, PT, PTT, fibrinogen (if available), and blood cultures

5. PPI (IV):

- Omeprazole (1 mg/kg daily); Esomeprazole (0-1 month: 0.5mg/kg OD; 1-11 months: 1mg/kg OD; 1-11 years and <20 kg: 10mg OD; 1-11 years and > 20kg 10-20mg OD; 12 years and above: 40mg OD.

6. Octreotide Dose:

- **Stat dose:** 1microgram/kg IV over 5 minutes (maximum 50 microgram) followed by Infusion at 1-3 µg /kg /hr. (max 50 µg /hour). Continue for 24 h after bleeding is controlled. Do not stop suddenly.

7. Vitamin K:

- 300microgram/kg as slow IV injection (max 10mg)

8. Intravenous Antibiotics:

- A third-generation cephalosporin or piperacillin/tazobactam depending on local guideline.

9. Platelet Transfusion:

- When platelets <50×103/µl, and plasma transfusion when PT and PTT>1.5 normal.

10. Ryle (Nasogastric Tube):

- Do gastric lavage with cold saline to remove blood from the stomach.

11. Inform the Target Tertiary Referral Center

- About the details of the case with the hemodynamic status at presentation and after resuscitation. For those presenting with hemodynamic instability a notification about the case should be given to the surgical and radiological departments within the referral center.

12. When to Refer:

- If you don't have feasibility to do upper endoscopy, **Please Don't Refer Except After** hemodynamic stabilization.

13. Secondary Prophylaxis:

- Propranolol; dose: 0.5-1 mg/kg/12 hr. orally.

14. Decision for Use of Balloon Tamponade:

- Will depend on the findings and actions in the first endoscopy. endotracheal intubation should be used with balloon tamponade for the risk of aspiration.

15. Re-endoscopy:

- Will be done when initial endoscopy was considered suboptimal. However, when bleeding is severe, radiologic intervention or surgery are indicated.

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