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Standard Treatment Workflow (STW) for the Management of
ANTITUBERCULAR THERAPY RELATED HEPATITIS

PATIENT TO BE STARTED ON ATT

Risk factors for ATT Hepatitis
- History of underlying liver disease (jaundice, ascites, GI bleeding)
- Physical findings suggestive of liver disease (Splenomegaly, ascites, icterus, edema)
- Alcoholism
- Hypoalbuminemia and Malnutrition
- Elevated aminotransferases at baseline
- HIV
- IV drug abuse
- Elderly age

Yes

Evaluate for underlying liver disease
HBsAg, Anti-HCV, Ultrasound

Chronic Liver disease +

- Intensive education & counselling
- Modified ATT may be needed based on Child Pugh Status
- LFT monitoring

No CLD or Cirrhosis

- Start ATT
- Counsel about symptoms of ATT Hepatitis

No

START ATT

Diagnosis of ATT hepatitis Clinical symptoms present (abdominal pain, vomiting, unexplained fatigue, yellowing of sclera, altered sensorium)
- AST/ALT increased to 3 times of baseline/ULN
- Jaundice (Bilirubin 2 ULN)

No clinical symptoms
- AST/ALT increased to 5 times of baseline/ULN

Exclude viral hepatitis (HBsAg, Anti-HCV, IgM- antiHAV, IgM-AntiHEV, Get PT/INR, Ultrasound liver

Stop all hepatotoxic drugs
- **Need urgent ATT:** Change to non-hepatotoxic drugs (Fluroquinolones, ethambutol & aminoglycosides)
- **No need for urgent ATT:** repeat LFT after a week & reintroduce (see later)
- **Non-resolution of LFT abnormalities:** exclude alternative causes of liver disease

Jaundice and coagulopathy/encephalopathy
- Refer to higher center immediately

Urgent ATT: life or organ threatening	No need for urgent ATT
• Sputum + Pulmonary TB • TB meningitis or CNS TB • Pericardial TB • Any form that is life threatening, eg., Intestinal TB with intestinal obstruction • Ocular TB • Joint or Spinal TB	• Sputum-ve Pulmonary TB • TB lymphadenitis • Tubercular pleural effusion • Tubercular ascites • Intestinal TB • Genitourinary TB • Bone TB

REINTRODUCTION OF ATT HEPATOXIC DRUGS

- Reintroduce only if ALT and AST < 2 ULN & normal bilirubin
- Start one drug at time: helps identify the culprit
- Rifampicin may be introduced at 10 mg/kg dose
- After one week add Isoniazid 5 mg/kg if LFT normal
- After one week add pyrazinamide 25 mg/kg if LFT is normal
- If ATT hepatitis severe (liver failure, coagulopathy or altered sensorium): Pyrazinamide reintroduction may be avoided
- Another approach could be low dose of one drug followed by full dose after three days
- Duration of ATT: count only when full ATT is started

REINTRODUCTION OF ATT: IF AST AND ALT < 2 ULN

SEQUENTIAL

Initiate one at a time Rifampicin 10 mg/kg

1 week: repeat LFT

Initiate Isoniazid 5 mg/kg

1 week: repeat LFT

Initiate Pyrazinamide 25 mg/kg

INCREMENTAL

Initiate Rifampicin 150 mg/day
Gradually increase dose by day 4

Initiate Isoniazid 100 mg/day at day 8
Gradually increase dose by day 11

Initiate Pyrazinamide 500 mg/day on day 15
Gradually increase dose by day 18

CHILD PUGH (CTP) SCORE

	Score 1	Score 2	Score 3
Bilirubin	**< 2 mg/dl**	**2-3 mg/dl**	**>3 mg/dl**
Albumin	**>3.5 gm/dl**	**2.8-3.5 gm/dl**	**<2.8 gm/dl**
INR	**<1.7**	**1.7-2.2**	**>2.2**
Ascites	**Absent**	**Slight**	**Moderate**
Encephalopathy	**Absent**	**Grade 1-2**	**Grade 3-4**

HEPATIC ENCEPHALOPATHY GRADE
- **Grade 0**: normal consciousness, personality & neurological examination
- **Grade 1**: restless, disturbances in sleep, irritability or agitated, tremors, handwriting affected
- **Grade 2**: lethargy, disorientation to time, asterixis, ataxia
- **Grade 3**: somnolent & stuporous, disoriented to place, hyperactive reflexes, rigidity
- **Grade 4**: unrousable coma, decerebrate

ATT SELECTION FOR UNDERLYING LIVER DISEASE

Child Status	Suggested ATT
Child A Cirrhosis (Score 1-6) Stable Liver disease	9 months of therapy with HRE **OR** 2 months of therapy with HRE followed by 7 months of HR
Child B Cirrhosis (Score 7-10) Advanced Liver Disease	One hepatotoxic drug regimen can be used: Two months of therapy with INH (or) RIF with ETH & aminoglycoside, followed by 10 months of therapy with INH/RIF & ETH
Child C Cirrhosis (Score 11-15) Very advanced liver disease	No hepatotoxic drug 18 to 24 months treatment using a combination of ETH, FQL, cycloserine & aminoglycoside/ capreomycin
In Acute hepatitis	Avoid hepatotoxic drugs ATT with non-hepatotoxic drugs if urgent ATT required Wait till improvement in liver function if no urgent need of ATT

ABBREVIATIONS

ALT: Alanine transaminase
AST: Aspartate transaminase
ATT: Anti-tubercular treatment
ETH: Ethambutol
FQL: Fluoroquinolone
GI: gastro-intestinal
HAV: Hepatitis A virus
HBsAg: Hepatitis B surface Antigen
HCV: Hepatitis C virus
HEV: Hepatitis E virus
HRE: Isoniazid, Rifampicin, Pyrazinamide
IgM: Immunoglobulin M
INH: Isoniazid
INR: International normalized ratio
IV: Intravenous
LFT: Liver function tests
PT: Prothrombin time
RIF: Rifampicin
TB: Tuberculosis
ULN: Upper limit of normal

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