Fatty Liver, Cholelithiasis and Obesity

These three conditions are closely related to **metabolic dysfunction, insulin resistance, dyslipidaemia and excess adiposity**, although each has distinct pathology and clinical features.

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1. Fatty Liver

Definition

Fatty liver (hepatic steatosis) is excessive accumulation of triglycerides within hepatocytes, conventionally involving **>5% of hepatocytes**.

It may occur because of alcohol, metabolic dysfunction, drugs, nutritional disorders or other causes.

The term **metabolic dysfunction-associated steatotic liver disease (MASLD)** is now used for steatotic liver disease associated with metabolic risk factors when significant competing causes are excluded.

Pathogenesis

A simplified mechanism is:

Obesity/insulin resistance
↓
↑ free fatty acid delivery to liver

- ↑ hepatic fatty-acid synthesis
  ↓
  Triglyceride accumulation in hepatocytes
  ↓
  Steatosis

In some patients:

Steatosis → hepatocellular injury/inflammation → fibrosis → cirrhosis

The inflammatory form is termed **metabolic dysfunction-associated steatohepatitis (MASH)**.

Risk factors

- Obesity, particularly central obesity
- Type 2 diabetes mellitus
- Insulin resistance
- Dyslipidaemia
- Metabolic syndrome
- Sedentary lifestyle
- Alcohol excess
- Certain drugs
- Rapid weight loss/malnutrition

Clinical features

Many patients are asymptomatic.

Possible findings:

- Fatigue
- Dull right upper-quadrant discomfort
- Hepatomegaly
- Abnormal liver enzymes
- Features of metabolic syndrome

Investigations

Liver function tests

- ALT and AST may be elevated
- GGT may be elevated
- Advanced disease may show reduced albumin and prolonged PT/INR

Metabolic evaluation

- Fasting glucose/HbA1c
- Lipid profile
- Blood pressure
- BMI and waist circumference

Imaging

- Ultrasound may show a bright/echogenic liver.
- Transient elastography can assess liver stiffness and steatosis.
- MRI-based techniques can quantify liver fat more accurately.

Complications

Steatosis → MASH → fibrosis → cirrhosis → hepatocellular carcinoma

Not every patient with fatty liver progresses to advanced liver disease.

Management

- Weight reduction when overweight/obese
- Regular physical activity
- Healthy dietary pattern
- Control diabetes
- Control dyslipidaemia and hypertension
- Avoid or minimize alcohol where appropriate
- Treat established advanced liver disease appropriately

A sustained weight loss of approximately **7–10%** can produce meaningful improvement in steatohepatitis and liver fibrosis in appropriate patients.

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2. Cholelithiasis

Definition

Cholelithiasis means the presence of **gallstones in the gallbladder**.

Gallstones are mainly:

1. **Cholesterol stones**
2. **Pigment stones**

A. Cholesterol stones

More common in many Western populations and increasingly encountered with metabolic risk factors.

Pathogenesis:

Supersaturation of bile with cholesterol
↓
Cholesterol crystal formation
↓
Gallbladder hypomotility/stasis
↓
Stone formation

Risk factors include:

- Obesity
- Female sex
- Increasing age
- Pregnancy

- Rapid weight loss
- Diabetes
- Dyslipidaemia
- Certain ethnic/genetic factors

B. Pigment stones

Black pigment stones

Associated particularly with:

- Chronic hemolysis
- Cirrhosis
- Increased bilirubin load

Brown pigment stones

Associated particularly with:

- Biliary infection
- Biliary stasis
- Bile duct pathology

Clinical features

Asymptomatic gallstones

Many gallstones are discovered incidentally and cause no symptoms.

Biliary colic

Typical features:

- Sudden severe right upper-quadrant or epigastric pain
- May radiate to the right shoulder/back
- Often occurs after a fatty meal
- Usually lasts several hours
- May be associated with nausea/vomiting

Complications

Complication	Important feature
Acute cholecystitis	Persistent RUQ pain, fever, Murphy sign
Choledocholithiasis	Stone in common bile duct

Obstructive jaundice	Conjugated hyperbilirubinaemia
Ascending cholangitis	Fever + jaundice + RUQ pain
Gallstone pancreatitis	Acute pancreatitis due to biliary obstruction
Gallbladder empyema	Suppurative infection
Gallstone ileus	Intestinal obstruction from an enteric fistula

Investigations

Ultrasound is the first-line imaging investigation for suspected gallstones.

May demonstrate:

- Gallstones
- Gallbladder wall thickening
- Pericholecystic fluid
- Biliary dilatation

If common bile duct obstruction is suspected:

- Bilirubin
- ALP
- GGT
- AST/ALT
- MRCP/EUS or other appropriate imaging

Management

- **Asymptomatic gallstones:** usually observation unless there is a specific indication for intervention.
- **Symptomatic gallstones:** laparoscopic cholecystectomy is commonly used.
- Complications require appropriate urgent management.

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3. Obesity

Definition

Obesity is excessive accumulation of body fat that adversely affects health.

BMI classification for adults

BMI=Weight (kg)Height2 (m2)\boxed{BMI=\frac{Weight\ (kg)}{Height^2\ (m^2)}}

BMI	WHO classification
<18.5	Underweight
18.5–24.9	Normal
25.0–29.9	Overweight
≥30	Obesity

For **Asian Indian populations**, cardiometabolic risk can occur at lower BMI values; therefore, lower action points are commonly used in Indian clinical practice.

Central obesity

Abdominal/visceral adiposity is particularly important because visceral fat is metabolically active.

Assessment includes:

- Waist circumference
- BMI
- Waist-to-height ratio
- Body composition where appropriate

For South Asian populations, commonly used waist cut-offs are approximately:

- **Men ≥90 cm**
- **Women ≥80 cm**

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4. Causes and pathogenesis of obesity

Obesity results from a chronic imbalance between **energy intake and energy expenditure**, modified by biological, environmental and behavioural factors.

Important factors

- Excess caloric intake
- Sedentary lifestyle
- Genetic susceptibility
- Sleep disturbance
- Endocrine disorders

- Certain medications
- Psychological/social factors
- Food environment

Adipose tissue is an endocrine organ

Adipose tissue produces adipokines and inflammatory mediators.

Excess visceral adiposity contributes to:

Insulin resistance → hyperinsulinaemia → metabolic dysfunction

and is associated with:

- Dyslipidaemia
- Hypertension
- Type 2 diabetes
- Fatty liver
- Cardiovascular disease

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5. Clinical consequences of obesity

Metabolic

- Insulin resistance
- Type 2 diabetes mellitus
- Dyslipidaemia
- Metabolic dysfunction-associated steatotic liver disease

Cardiovascular

- Hypertension
- Coronary artery disease
- Heart failure
- Stroke

Respiratory

- Obstructive sleep apnoea
- Obesity hypoventilation syndrome

Musculoskeletal

- Osteoarthritis
- Back problems

- Reduced mobility

Gastrointestinal/hepatobiliary

- Gallstones
- Fatty liver
- Reflux disease

Reproductive

- Menstrual dysfunction
- Infertility
- Pregnancy complications

Malignancy

Obesity is associated with increased risk of several cancers, including endometrial, postmenopausal breast, colorectal and some other cancers.

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6. Relationship between obesity, fatty liver and gallstones

A useful MBBS concept is:

Obesity / visceral adiposity
↓
Insulin resistance + altered lipid metabolism
↓↓
Hepatic triglyceride accumulation → Fatty liver
↓
Increased cholesterol secretion into bile + gallbladder dysfunction
↓
Cholesterol gallstone formation

Thus, obesity can contribute to **both hepatic steatosis and cholesterol cholelithiasis**, although the mechanisms are not identical.

High-yield comparison

Feature	Fatty liver	Cholelithiasis	Obesity

Primary problem	Hepatic fat accumulation	Gallstones	Excess adiposity
Major association	Insulin resistance/metabolic dysfunction	Cholesterol supersaturation/stasis	Energy imbalance + metabolic dysfunction
Common presentation	Often asymptomatic	Often asymptomatic; biliary colic if symptomatic	Usually apparent by anthropometry
Key investigation	LFT + ultrasound/elastography	Ultrasound	BMI + waist circumference
Major complications	MASH, fibrosis, cirrhosis, HCC	Cholecystitis, CBD stone, cholangitis, pancreatitis	Diabetes, CVD, OSA, fatty liver
Major intervention	Lifestyle/metabolic risk management	Cholecystectomy if symptomatic/complicated	Lifestyle ± pharmacological/surgical treatment when indicated

Viva pearls

- **Fatty liver:** triglyceride accumulation in hepatocytes.
- **MASH:** steatosis accompanied by hepatocellular injury and inflammation.
- **Most common gallstones:** cholesterol stones in many populations.
- **Best initial investigation for gallstones:** ultrasonography.
- **Typical pain of biliary colic:** right upper quadrant/epigastric, often after fatty meals.
- **Obesity:** BMI ≥30 kg/m² by the standard WHO adult classification.
- **Most metabolically important fat:** visceral/abdominal fat.
- **Important metabolic triad:** obesity + insulin resistance + dyslipidaemia.
- **Major long-term concern in fatty liver:** progressive fibrosis and cirrhosis in susceptible individuals.