7.3.2.2. Hyperuricemia

A condition of **excess uric acid in the blood** is termed **hyperuricemia**. Uric acid passes through the liver and reaches the bloodstream. Maximum amount of uric acid is excreted in the form of urine (i.e., removed from the body through urinary system) or as intestinal excretion. This aids in maintaining normal levels of uric acid in the human body.

Causes

Hyperuricemia can be primary (increased ~~uric acid levels~~ due to purine) and secondary (increased uric acid levels due to another disease or condition) depending on the cause:

1) **Primary Hyperuricemia**
   i) In this condition, uric acid is produced in large amounts due to purines, and
   ii) Renal excretion of uric acid does not occur, thus, its concentration in blood increases.
2) **Secondary Hyperuricemia**
   i) Cancers or the chemotherapeutic agents used may increase the rate of cell death which results in high uric acid levels.
   ii) A rapid amount of cellular destruction and tumour lysis syndrome occur after chemotherapy.
   iii) A renal disorder can result in hyperuricemia due to failure of uric acid renal excretion.
   iv) Some medications result in hyperuricemia.
   v) Endocrine or metabolic disorders (diabetes or acidosis) may result in hyperuricemia.
   vi) Increased uric acid levels result in kidney problems or none at all.

Symptoms

1) In some cases, no symptoms occur at all.
2) A hyperuricemic patient going through leukaemia or lymphoma chemotherapy may experience the symptoms of kidney problems or gouty arthritis.
3) A hyperuricemic patient having certain forms of cancer experiences fever, chills, and weakness.
4) In a hyperuricemic patient, deposition of uric acid crystals on a joint results in gout (i.e., inflammation of the joint).
5) In a hyperuricemic patient, kidney stones may occur (which further leads to renal disorders).
6) A hyperuricemic patient also experiences problem while urinating.

Diagnosis

Blood and urine tests are recommended by the doctor to determine the levels of creatinine (for determining kidney function) and uric acid.

Treatment

Hyperuricemia is treated on the basis of its causes. If asymptomatic, it is not treated. In this condition, there is not any proven benefit to administer uric acid lowering therapies. If an underlying condition has resulted in hyperuricemia, it is treated with medicines and by changing diet in order to reduce the blood levels of uric acid.

7.3.2.3. Gout Disease

Purines (ingested through food) breakdown to produce uric acid. When this uric acid (monosodium urate) accumulates within the tissues in excessive amounts, it results in a disorder termed as **gout**. It is clinically manifested in the form of painful joints and is the most common inflammatory joint disease.

Types

1) **Primary Gout:** This category includes gout that occurs due to unknown reasons or that results from inborn errors of metabolism. It primarily manifests as hyperuricemia and gout.

2) **Secondary Gout:** This category includes gout that occurs as a result of an underlying abnormality.

   However, it is not always associated with manifestation of gout and may only be manifested as hyperuricemia.

Causes

1) **Primary Gout:** The cause for primary form of gout is **unknown**. However, **genes** and **environmental factors** cause gout as a result of a defect in the metabolism of purines.

2) **Secondary Gout:** It may arise due to:
   i) Secondary gout occurs as one of the manifestations of an **underlying disease process** due to the breakdown of nucleic acid resulting in hyperuricemia. The diseases include hypertension, diabetes mellitus, obesity, renal disease, sickle cell anaemia, or a chronic kidney disease.
   ii) It may result as a **side effect** of **certain drugs** like hydrochlorothiazide, or pyrazinamide in which the excretion of uric acid in its ionic form is decreased, thus, resulting in hyperuricemia.
   iii) Consumption of **other drugs** like low dose acetylsalicylic acid, cytotoxics and ethambutol.
   iv) Drugs like thiazides that interfere with the excretion of uric acid may also lead to gout.

Symptoms

1) **Asymptomatic Stage:** Initially, the patient is asymptomatic. The disease however begins and is manifested as hyperuricemia (though the deposition of crystal in the tissues begins, it does not cause pain as yet).

2) **Acute Stage:** This phase is characterised by:
   i) The characteristic acute attack of gout is monoarticular, i.e., affects a single joint, (usually a single large joint) but oligo-articular and

polyarticular gout can also occur, particularly in elderly patients. Generally, the first joint to be affected is the metatarsophalangeal (MTP) joint. However, the tarsal joints, heels, knees, wrist, fingers, and the elbow may also be affected initially.

ii) The acute episode usually begins at night. The onset of pain is abrupt. Aggravating factors for the pain include factors such as excessive exercise, food, alcohol consumption, certain medications, dieting, or even the weight of a bed sheet.

iii) Severe pain develops rapidly. The joint becomes very tender reaching its maximum severity within 6-24 hours of onset.

iv) Redness and inflammation (swelling) of the area may be observed. Sometimes, low grade fever may be present. The acute phase may resolve spontaneously after continuing for days or weeks together.

3) **Intercritical Stage:** This is the early stage of gout once the initial attack has subsided. In this stage, the patient remains asymptomatic for a long period of time (even months or years) and it may even happen that the next attack never occurs.

4) **Chronic Stage:** This phase is characterised by:
   i) Presence of hyperuricemia,
   ii) Chronic arthritis,
   iii) Sore and painful joints,
   iv) Formation of tophus (large, hard nodules formed as a result of deposition of urate crystals in soft tissue), and
   v) Recurrent attacks of acute gout.

Diagnosis

1) **Laboratory Assays:** Blood and urine tests are performed to determine the level of uric acid in order to detect hyperuricaemia (in patients with primary gout, the level of uric acid in urine is higher than in patients with secondary gout).

2) **Imaging:** Imaging techniques involves X-rays. Initially gout cannot be detected by X-rays. However, at later stages, the articular cartilage and subchondral bones are destroyed. The overhanging margins of bony contour are outwardly displaced.

3) **Synovial Biopsy:** This is the gold standard for diagnosis of gout. Monourate crystals (or monosodium urate crystals) in the form of needles are seen in the **tophaceous deposits** collected either from synovial fluid or from tissue sections.

Treatment

1) **Non-Pharmacological Approach:** Non-pharmacological measures helped to reduce the levels of uric acid and thus decrease the frequency and severity of recurrence. The measures include:
   i) Maintenance of ideal weight,
   ii) Moderation in alcohol consumption,

iii) Avoiding food rich in purines (**e.g.,** meat, peas, lentils, sweetbread etc.),
iv) Increasing fluid intake (to dilute the amount of uric acid in blood), and
v) Avoiding drugs that inhibit the excretion of uric acid (**e.g.,** thiazide diuretics, low-dose aspirin).

2) **Pharmacological Approach:** Analgesics, anti-inflammatory drugs, uricosurics, and inhibitors of uric acid synthesis are prescribed for the treatment of gout, as mentioned below:

i) **Analgesics and Anti-Inflammatory Drugs:** The principal anti-inflammatories and analgesics used for the treatment of acute gout are Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), corticosteroids, and colchicine.

ii) **Uricosurics:** Uricosurics are drugs that increase the clearance of uric acid. Probenecid is a uricosuric used in the treatment of gout.

iii) **Inhibitors of Uric Acid Synthesis:** It includes drugs that block the final enzymatic step in the synthesis of uric acid, **e.g., xanthine oxidase inhibitors**. Drugs used under xanthine oxidase inhibitors are allopurinol and febuxostat.

iv) **Metabolism of Uric Acid:** It consists of a new class of drugs used for the treatment of chronic gout and mainly involves drugs of class **recombinant urate oxidase enzymes**. **Examples** of recombinant urate oxidase enzymes include pegloticase, and rasburicase.