Chapter—2 (E) Pharmacotherapeutics
Gastro intestinal system

Introduction— The gastrointestinal (GI) tract is a hollow tube extending from the oral cavity to the anus that consists of anatomically distinct segments, including the oesophagus, stomach, small intestine, colon, rectum, and anus. Each of these segments has unique, complementary, and highly integrated functions, which together serve to regulate the intake, processing, and absorption of ingested nutrients and the disposal of waste products.

Clinical consideration—

- Irritable bowel syndrome.
- Hypertrophic pyloric stenosis.
- Oesophageal achalasia.
- Gastro oesophageal reflux disease (GERD).
- Peptic ulcer/gastric ulcer/duodenal ulcer.
- Inflammatory bowel diseases (IBDs).
- Alcoholic liver disease etc.

Gastro oesophageal reflux disease (GERD)

Definition— GERD also known as acid reflux, is most common in individuals older than age 40 but also occurs in infants and children. Symptoms are often worse at night, when lying supine, or after consuming foods or drugs that diminish lower oesophageal sphincter tone, such as caffeinated beverages. The stratified squamous epithelium of the oesophagus is resistant to abrasion from foods but is sensitive to acid. Submucosal glands, which are most abundant in the proximal and distal oesophagus, contribute to mucosal protection by secreting mucin and bicarbonate. More importantly, the tone of the lower oesophageal sphincter prevents reflux of acidic gastric contents, which are under positive pressure and would otherwise enter the oesophagus. Reflux of gastric contents into the lower oesophagus is the most frequent cause of GERD (Gastro oesophageal reflux disease).

Etiopathogenesis—

- The most common cause of gastroesophageal reflux is transient lower oesophageal sphincter relaxation. This is thought to be mediated via vagal pathways, and can be triggered by gastric distention, by gas or food, mild pharyngeal stimulation that does not trigger swallowing, and stress.
- Gastroesophageal reflux can also occur due to forceful opening of a relatively hypotensive lower oesophageal sphincter by an abrupt increase in intraabdominal pressure, such as that due to coughing, straining, or bending.
- Other conditions that decrease lower oesophageal sphincter tone or increase abdominal pressure and contribute to GERD include alcohol and tobacco use, obesity, central nervous system depressants, pregnancy, hiatal hernia, delayed gastric emptying, and increased gastric volume.

Clinical manifestations—

- Burning sensation in the chest region (Heart burn).
- Regurgitation (Backflow of food or liquid).
- Dysphagia (Trouble swallowing).
- Sensation of a lumb in throat.
- Barrett oesophagus (Chronic recurrent reflux can also result in a change in the oesophageal epithelium from squamous to columnar histology).

Pharmacological managements— Omeprazole, Rabeprazole, Pantoprazole, esomeprazole, Lansoprazole, dexlansoprazole etc.

Non-pharmacological management—

- Maintain/regulate the food intake (time to time) and take food after proper digestion of the previous food.
- If any complication appears and consults with doctors and make the diet charts and fallow strictly.
- Water help the regulating the acid reflex and helps in digestion, so water consumption also maintain the GERD.
- Sleeping/sitting posture also important for maintaining the GERD.
- Follow regular yoga and exercise according to need because physically activity also helps in the digestive activity.
- Electrolytes are also very important in this condition.
- Avoid more species food and diet (because it cause acidity).

Peptic Ulcer Disease.

Definition— Peptic ulcer disease (PUD) refers to chronic mucosal ulceration affecting the duodenum or stomach. Nearly all peptic ulcers are associated with *Helicobacter pylori* infection, NSAIDs, or cigarette smoking. PUD results from imbalances between mucosal defence mechanisms and damaging factors that cause chronic gastritis. Thus, PUD generally develops on a background of chronic gastritis. Gastric peptic ulcers are predominantly located along the lesser curvature near the interface of the body and antrum. Peptic ulcers are solitary in more than 80% of patients.

Etiopathogenesis—

- Various causes of absolute or relative increased acid production or decreased mucosal defences predispose to acid-peptic disease.
- Bacterium *Helicobacter pylori* is the root cause of a number of forms of acid-peptic disease, including duodenal ulcer, gastric ulcer, and gastritis. It can cause acid-peptic disease by multiple mechanisms, including direct alteration of signal transduction in mucosal and immune cells, which in turn can increase acid secretion and diminish mucosal defences.
- PUD may also be caused by acid secreted by ectopic gastric mucosa within the duodenum or an ileal Meckel diverticulum. PUD may also occur in the oesophagus as a result of GERD or acid secretion by oesophageal ectopic gastric mucosa (an inlet patch).

Clinical manifestations—

- Epigastric burning or aching pain.
- Iron deficiency anaemia.
- Haemorrhage/ GI tract bleeding.
- Hematemesis (vomiting of blood).
- Melena (tarry stools from the effect of acid on blood).
- Perforation and infections.

Pharmacological managements—

- Prostaglandin analogues. Ex- misoprostol, rioprostil.
- H_2 receptor antagonists. Ex- ranitidine, famotidine, cimetidine.
- Proton pump inhibitors. Ex- Omeprazole, Rabeprazole, Pantoprazole.
- Anti- cholinergics. Ex- anistropine, hyoscyamine.

Non-pharmacological management—

- Maintain/regulate the food intake (time to time) and take food after proper digestion of the previous food.
- If any complication appears and consults with doctors and make the diet charts and fallow strictly.
- Change the life style and take the warm water.
- Follow regular yoga and exercise according to need because physically activity also helps in the digestive activity.
- Electrolytes are also very important in this condition.
- Avoid more species food and diet (because it cause acidity).
- Avoid smoking and alcohol consumption.

Alcoholic liver disease

Definition— Alcohol (ethanol) is the most useful chemical agent in the pharmaceutical industry for the preparation of the drugs, as well as it is also used as the solvents. Now a days alcohol consumption is common in our traditional culture but regular practice of alcohol leads to the addiction and cause the many types of disease (heart disease, liver disease, G.I.T infections, lungs disease etc).

Alcoholic liver disease is a chronic disorder that can give rise to steatosis, alcoholic hepatitis, progressive steatofibrosis and marked derangement of vascular perfusion leading eventually to cirrhosis. Consumption of 80 gm/day of alcohol is considered to be the threshold for the development of alcoholic liver disease.

Excessive alcohol (ethanol) consumption is the leading cause of liver disease it is accounts for 3.8% of deaths globally, making it the eighth highest risk factor for death.

Etiopathogenesis—Short-term ingestion of as much as 80 gm of alcohol over one to several days generally produces mild, reversible hepatic steatosis. Daily intake of 80 gm or more of ethanol generates significant risk for severe hepatic injury, and daily ingestion of 160 gm or more for 10 to 20 years is caused severe injury. There are three manifested stages discussed-

1. **Hepatocellular steatosis (fatty liver)—** It is the initial condition arises due to the due to moderate consumption of alcohol, in this condition lipids droplets getting accumulate in the hepatocytes cell and finally small droplets coalesce into large droplets.
   Macroscopically, the fatty liver in individuals with chronic alcoholism is a large (as heavy as 4 to 6 kg), soft organ that is yellow and greasy. **Fatty change is completely reversible if there is abstention from further intake of alcohol.**

2. **Alcoholic hepatitis**— it is characterized by-
   - Hepatocyte swelling and necrosis— The swelling results from the accumulation of fat and water, as well as proteins that are normally exported.
   - Mallory-Denk bodies—These are usually present as clumped, amorphous, eosinophilic material in swell hepatocytes. It is not specific feature of alcoholic liver disease, since they are also present in non-alcoholic fatty liver disease also.
   - Neutrophilic reaction— Neutrophils permeate the hepatic lobule and accumulate around degenerating hepatocytes, particularly those having Mallory-Denk bodies.
3. **Alcoholic steatofibrosis (cirrhosis)—**Alcoholic hepatitis is often accompanied by prominent activation of sinusoidal stellate cells and portal fibroblasts, giving rise to fibrosis. Fibrosis begins with sclerosis of central veins.

Clinical manifestations—

- Abdominal swelling.
- Jaundice
- Haematological disorders
- Indigestion and constipation.
- Fainting and mental disturbance.
- Renal disorders.

Pharmacological managements— Metadoxine, deoxycholic acid, ursodiol, l-arginine, obeticholic acid.

Non-pharmacological management—

- Maintain/regulate the food intake (time to time) and take food after proper digestion of the previous food.

- If any complication appears and consults with doctors and make the diet charts and fallow strictly.
- Change the life style and take the warm water.
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Inflammatory Bowel Diseases (Crohn's Disease and Ulcerative Colitis).

Definition—Inflammatory bowel disease (IBD) is distinguished from infectious entities by exclusion and by chronicity due to the inappropriate mucosal immune activation. Patients often experience recurrent episodes of mucopurulent (containing mucus and white cells), bloody diarrhoea due to pathogens and failure to respond to antibiotics alone. The two disorders that comprise IBD are Crohn's disease and ulcerative colitis. The distinction between ulcerative colitis and Crohn disease is based, in large part, on the distribution of affected sites and the morphologic expression of disease at those sites.

a. **Crohn's disease—Crohn disease**, which has also been referred to as regional enteritis (because of frequent ileal involvement) may involve any area of the GI tract (including the oral cavity, oesophagus, stomach, and proximal small intestine). The combination of deep mucosal ulceration and submucosal thickening gives the involved mucosa a characteristic "cobblestone" appearance.
    - In this condition intestinal lesions are appeared in skip manner like (patches of lesion) and transmural inflammation, ulcerations and fissures are present.
b. **Ulcerative colitis—Ulcerative colitis** is limited to the colon and rectum and extends only into the mucosa and submucosa. It typically begins at the anorectal junction and extends proximally
    - In this condition intestinal lesions are appeared in continuous manner (mainly in colonic and rectum) and pseudo polyp mucosal ulcer are present.

Etiopathogenesis—

- The two disorders that comprise IBD are ulcerative colitis and Crohn's disease.

- Most investigators believe that IBD results from the combined effects of alterations in host interactions with intestinal microbiota, intestinal epithelial dysfunction, aberrant mucosal immune responses, and altered composition of the gut microbiome. Most of the condition mucosal immune activation and defective immunoregulation contribute to the development of ulcerative colitis and Crohn disease.

Clinical manifestations—

a. **Crohn's disease**
   - Arthritis (inflammatory disorders of the joints).
   - Erythema nodosum (skin disorder).
   - In eye (uveitis, iritis).
   - Aphthous ulcers of the buccal mucosa.
   - In bile ducts (sclerosing cholangitis).
   - In liver (autoimmune chronic active hepatitis)
   - Renal disorders, especially nephrolithiasis.
   - Amyloidosis is a serious complication of Crohn disease

b. **Ulcerative colitis.**
   - Obstructions
   - Perforations.
   - Fistula formation.
   - Infections.

Pharmacological managements— alosetron, lubiprostone, rifaximin, loperamide, linaclitide, tenapanor, eluxadoline, Azathioprine,mercaptopurine.

Non-pharmacological management—

- Maintain/regulate the food intake (time to time) and take food after proper digestion of the previous food.
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