Acute Pancreatitis in pregnancy

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Introduction:

Acute pancreatitis (AP) is a common acute medical condition requiring emergent care. The exact prevalence in India is not known. The condition is prevalent in western countries.[1]

AP during pregnancy is a rare but severe clinical problem causing significant maternal and perinatal mortality and morbidity. A multidisciplinary approach, including gastroenterologist, surgical and obstetric care is essential to manage it effectively.[2]

AP is rare, occurring in 1 in 1000 to 1 in 12000 pregnancies. It is more common in multigravidas (75%) occurring commonly in the third trimester (50%) and postpartum period (38%) and is relatively uncommon in the first trimester (12%).[3]

Causes of Acute Pancreatitis in pregnancy:

1. Gall stone diseases-It is associated in 65-100% cases. The incidence of biliary manifestations during pregnancy (colic, acute cholecystitis, cholangitis, or biliary AP) is from 0.05 to 8%. In a prospective study of over 3000 patients, who had ultrasound examinations throughout the pregnancy, the authors showed a cumulative incidence of sludge or gallstones in early postpartum in 10.2%, with biliary sludge in 5.1%, stones in 2.8% and gallstones in patients with pre-existing sludge in 2.3%. Asymptomatic biliary complications occurred in 1.2% of pregnant women.[3]
2. Hypertriglyceridemia
3. Alcohol-induced
4. Drugs- medications such as diuretics, anti-hypertensive agents, antibiotics e.g., Erythromycin, Mesalamine, Sulfasalazine, Acetaminophen, Didanosine, and steroids (6)
5. Hypercalcemia (Hyperparathyroidism)
6. Idiopathic

Table 1. Causes of AP in pregnant women

Gallstones (65–100%)
Alcohol abuse (5–10%)
Familial hypertriglyceridemia-induced pancreatitis (5%)
Idiopathic (15%)
Drugs-induced AP (thiazide diuretics) (cases)
Pancreatitis associated with pregnancy-induced hypertension (cases)
Acute fatty liver of pregnancy associated with AP (cases)
Hyperparathyrodism (cases)
Gene mutations (cases)
Cationic trypsinogen (PRSS1)
CFTR
PSTI
PPARG

Abbreviations: AP, acute pancreatitis; CFTR, cystic fibrosis transmembrane conductance regulator; PPARG, peroxisome proliferator-activated receptor gamma; PSTI, pancreatic secretory trypsin inhibitor.

(Acute pancreatitis during pregnancy , Journal of Perinatology)

Pathophysiology of Pancreatitis in Pregnancy:

GB disease

- increased cholesterol synthesis in second and third trimesters
- supersaturated bile
- delayed GB emptying due to progesterone effect
- increased pressure in the sphincter of Oddi
- sizeable residual volume of GB
- cholesterol crystals and GB stone formation.

Clinical symptoms of Acute Pancreatitis in pregnancy:

The incidence of biliary manifestations during pregnancy (colic, acute cholecystitis, cholangitis, or biliary AP is from 0.05 to 8%.

The pregnant woman presents with acute severe pain upper abdomen, radiating to the back (40%)., associated with vomiting, fever, epigastric tenderness on examination. In severe cases, the patient could be toxic with tachycardia and hyperventilation.

Diagnosis of Acute Pancreatitis

- CBC – raised total counts (Blood investigations could pose a challenge in interpretation as some of the levels are changed during normal pregnancy, like total counts, alkaline phosphatase).
- LFT, sugars, serum lipid profile
- Serum lipase (more specific), serum amylase, raised to 3 times normal.
- USG abdomen – GB stones. Safe and no radiation exposure.
- MRCP - Magnetic resonance cholangiopancreatography (MRCP) without contrast medium (gadolinium) is more specific. It can diagnose CBD stones and study pancreatic

parenchyma and duct in detail to rule out pseudocysts, inflammation etc. MRCP can help as a guide to remove stones too. It is safe and non-invasive.

- ES – endoscopic ultrasound – more sensitive for CBD stones, but GA is required for the test. More sensitive to diagnose CBD stone, if diagnosed, in the same sitting, ERCP with sphinctorotomy can be done

Assessment of severity of Acute Pancreatitis:

Since the morbidity and mortality differ markedly between mild and severe disease (mild < 5% v/s severe 20–25%), it is imperative to assess severity as early as possible. Multiple clinical criteria, biochemical parameters and imaging criteria have been used for this purpose. The risk scoring is based on CT scan findings, which is contraindicated in pregnancy. Therefore, severity has to be assessed clinically.

1. BISAP criteria-
   - BUN > 25
   - Impaired mental status
   - SIRS
   - Age >60 yrs (not applicable here)
   - Pleural effusion
2. Bedside assessment of severity

Mild disease

- Absence of rebound tenderness and guarding of the abdomen
- normal hematocrit
- normal creatinine

3. Ranson's criteria – (as in non-pregnant state) [3]

Table 2. Ranson's criteria for prognosis of acute pancreatitis

Ranson's criteria on admission:
Age >55 years
White blood cell count >16 000 cells mm^{-3}
Blood glucose >11 mmol l^{-1}
Serum AST >250 IU l^{-1}
Serum LDH >350 IU l^{-1}
Ranson's criteria after 48 h of admission:
Hypocalcemia (serum calcium <2.0 mmol l^{-1})
Fall in hematocrit by >10%
Hypoxemia (PO_2 <60 mm Hg)
Increase in BUN to >1.98 mmol l^{-1} after IV fluid hydration
Base deficit (negative base excess) >4 mmol l^{-1}
Sequestration of fluids >6 l
Interpretation
If the score ⩾3, severe pancreatitis likely
If the score <3, severe pancreatitis is unlikely
Or
Score 0–2: 2% mortality
Score 3–4: 15% mortality
Score 5–6: 40% mortality
Score 7–8: 100% mortality

Abbreviation: AST, aspartate aminotransferase; BUN, blood urea nitrogen; IV, intravenous; LDH, lactate dehydrogenase.

(Acute pancreatitis during pregnancy, Journal of Perinatology)

Prognostic markers: Indicators of poor prognosis are-

- BUN > 33 indicates pancreatic necrosis
- Obesity (BMI > 30)
- Plasma glucose greater than 190 mg/dL
- SIRS greater than or equal to 2
- Trypsinogen activated peptide (TAP), serum procalcitonin (> 3.8 ng/ml),
- C-reactive protein greater than 150 mg/L, coagulation parameters (e.g., d-dimer),
- Interleukin-6 (> 122 pg/ml)

MANAGEMENT OF AP IN PREGNANCY:

Management of Gall stone pancreatitis in pregnancy: It depends on :

- the trimester-

1. Conservative in the first trimester and lap cholecystectomy in the second trimester.
2. Lap cholecystectomy in the second trimester
3. Third trimester – conservative treatment or ERCP lap cholecystectomy in the early postpartum period.

- Severity of symptoms
- CBD impaction of stones.

Admission – All patients with AP have to admitted to the hospital to monitor vitals and to watch for cardiorespiratory distress for 48 hours. Worsening parameters may necessitate ICU care.

Conservative –pain relief/ nutrition/ fluid replacement
1.Analgesia- NSAIDS

2. Bowel Rest, IV fluids - **Fluid Therapy-** Adequate fluid replacement to maintain effective circulating volume and perfusion pressure is necessary to maintain pancreatic microcirculation. The fluid requirement may be quite large because of the substantial loss of fluid in the retroperitoneal space. CVP may be necessary to monitor fluid status. Fluid therapy should be enough to maintain urine output of 40-50ml/hr.

3.Nutrition –Acute pancreatitis is a hypercatabolic state. Enteral nutrition can be instituted within 24 hours of AP in the vast majority of patients. It is advisable to do so in a graduated manner, i.e., start with liquids and then advance to a soft diet and then to a regular diet.

Early enteral nutrition therapy

- modulates the stress response,
- helps in the early resolution of disease,

- decreases the risk of bacterial translocation and infection decreases tissue necrosis
- decreases surgical intervention and mortality risk
- results in a better outcome

4.Antibiotic therapy- no role of prophylactic antibiotics

5.Monitoring for complications

Interventions in Acute Pancreatitis in pregnancy:

An important decision is the choice of procedure to clear CBD stones. Second is the timing of the procedure and approach to cholecystectomy.

- This depends on the trimester of pregnancy
- Presence or absence of CBD dilatation and cholangitis
- Severity of AP

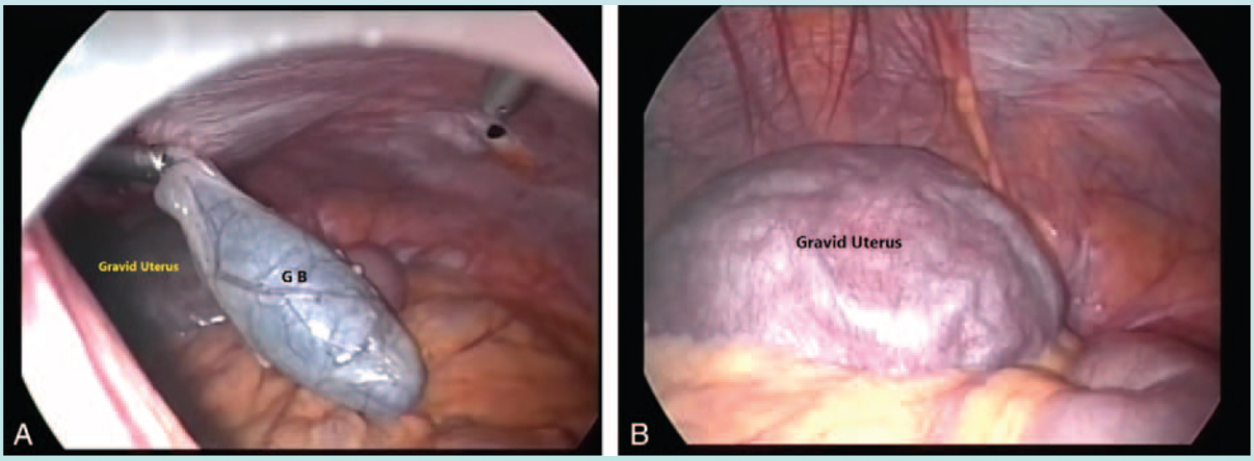
1.**Surgery** – Indications are

- Severe AP
- Obstructive jaundice
- Acute cholecystitis intractable to medical treatment and peritonitis.

Types of cholecystectomy – laparoscopic or Open.

Laparoscopic cholecystectomy is safe during pregnancy, particularly in the second trimester, as the fetal organogenesis is over and the uterus is not too large. It has the advantages of reduced hospital stay, decreased narcotic use and a quick return to regular diet as compared to open surgery.

The complications of laparoscopic surgery are uterine perforation during trocar placement, induction of preterm delivery, and fetal acidosis.



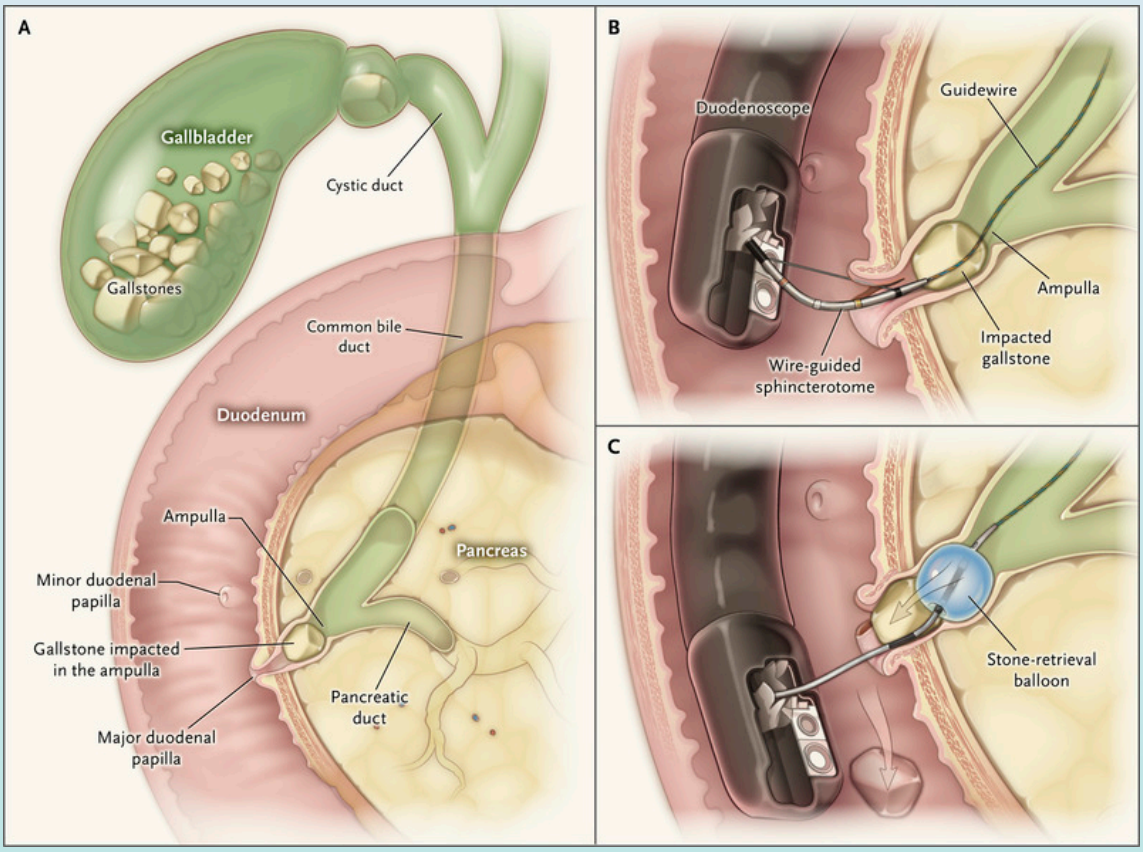
(Journal of Arab society of Medical Research)

2. ERCP (**Endoscopic Retrograde Cholangial-pancreatography**)**:**

Indications for ERCP with sphincterotomy and clearance of bile duct stones –

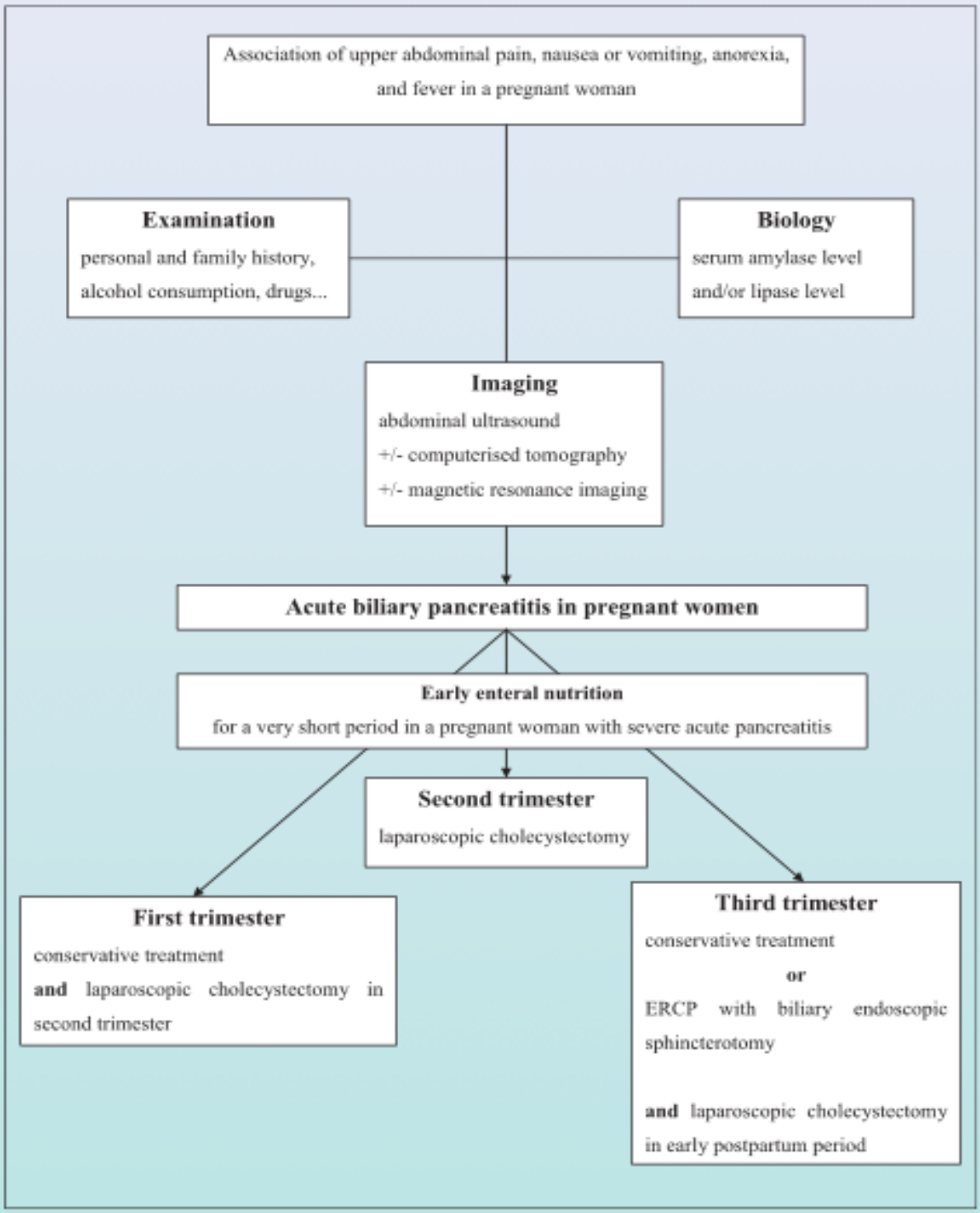
1. CBD stone obstruction causing severe AP
2. Postcholecystectomy pts with CBD stone
3. Patients in whom surgery is relatively contraindicated, plus first and third trimesters .[4]

- ERCP removes the impacted stones in CBD, thereby facilitating easy drainage of bile. It prevents cholestasis, prevents bacterial infection and improves symptoms.
- It is safe if fluoroscopy time is to limited with a lead shield to fetus and pelvis.
- Therapeutic ERCP is associated with significantly higher radiation exposure than diagnostic ERCP (12.4 mSv versus 3.1 mSv). Therefore fetal risks have to be considered before intervention with ERCP.
- Risks with ERCP – bleeding, perforation.
- ERCP helps in the prevention of recurrence of AP in the third trimester. (Acute Biliary Pancreatitis in pregnancy has a high recurrence rate - 70% vs 20 % in the non-pregnant population).



(ERCP for Gallstone Pancreatitis- The New England Journal of Medicine)

ALGORITHM FOR MANAGEMENT OF GB STONE CAUSING ACUTE PANCREATITIS IN PREGNANT WOMEN:



(Acute pancreatitis during pregnancy: a review. Journal of perinatology)

Acute Pancreatitis caused by Hyper triglyceridemia:

- Hypertriglyceridemia is common in pregnancy as there is 2-3 times increase in TG level, which peak during the third trimester, due to increased hepatic synthesis of very-low-density lipoproteins and a reduction in the activity of lipoprotein lipase concerning the high levels of estrogen.

Factors favouring dyslipidaemia disturbances are excessive weight gain, diabetes, alcohol consumption, drugs (steroids, diuretics, and beta-blockers), and latent genetic abnormalities (lipoprotein lipase, apoC2, or apoE).

- TG > 1000 mg /dl pose a high risk for pancreatitis.

AP caused by hypertriglyceridemia is more common in the third trimester. More severe than gall stone-induced AP, causing more complications in pregnancy.

Management of AP caused by HT:

- Dietary fat restriction
- Nutritional supplements
- In severe cases, therapeutic plasma exchange and/or combined heparin and insulin infusions to increase lipoprotein lipase activity are effective

Alcohol Induced AP In Pregnancy: Rare.

Alcohol is toxic to the pancreas in a dose-dependent manner. Apart from AP, alcohol use during pregnancy can cause abortion, growth restriction, birth defects, and as well as fetal alcohol syndrome.

Higher risk of preterm delivery (68%) and recurrent attacks.

Pseudocysts, if present, can be observed for six weeks as up to 40% of them can resolve spontaneously.

Management of alcohol-induced AP involves Multidisciplinary approach.

Proper Nutrition and medications are required and if near term, delivery is warranted.

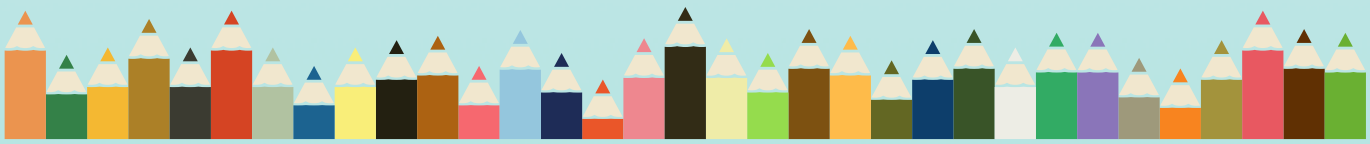
Complications of acute pancreatitis in pregnancy:

Non-gallstone pancreatitis as a whole has worse outcomes than uncomplicated gallstone pancreatitis.

1. Maternal complications-

Earlier – 20% **maternal deaths** and 50% **fetal loss**. (pre ERCP and Lap cholecystectomy era). Now mortality has reduced significantly 0 - <5%, owing to technical advances in imaging and therapeutic endoscopy. Other complications are-

- Recurrent Pancreatitis, Pancreatic Pseudocyst
- Diabetes
- generalized peritonitis
- Adult Respiratory Distress Syndrome (ARDS)
- Disseminated Intravascular Coagulation (DIC)



2. Fetal complications –
- Preterm labor and problems of prematurity
- IUD
- Patients who developed AP during the first trimester had the lowest percentage of term pregnancy (60%) and the highest risks of fetal loss (20%) and preterm delivery (16%).

Mode of delivery

A multidisciplinary approach including gastroenterologists, surgeons and obstetricians is preferred.
No standardized guidelines regarding the mode of delivery are in place.
If the disease is mild and vaginal delivery is possible, it is preferable to do so.
Cesarean can increase the risk of superinfection.

Chronic pancreatitis and pregnancy:

Chronic pancreatitis is diagnosed when episodes of pancreatitis occurred over many years, accompanied by a diagnosis of chronic pancreatitis or with evidence of pancreatic insufficiency (diabetes) or surgical intervention (Roux-en-Y).
Alcohol-induced more common (58%)
Risk of recurrence and preterm delivery

Conclusion: Pancreatitis is an important clinical entity in pregnancy with varied causes. Timely diagnosis, early treatment and prompt interventions can prevent maternal and fetal morbidity and mortality.

References:

1. Management of Acute Pancreatitis: Indian Guidelines and Protocol, Rakesh K Tandon. Gastroenterology
2. Hepatobiliary Pancreatic Dis Int, Vol 15,No 4 • August 15,2016 • Www.Hbpdint.Com .Pancreatitis In Pregnancy: Etiology, Diagnosis, Treatment, And Outcomes. Padmavathi Mali & Marshfield, USA
3. Acute pancreatitis during pregnancy. Ducarme et al. Journal of Perinatology (2014), 87 – 94 & 2014 Nature America, Inc.
4. Acute pancreatitis in pregnancy .Capecomorin S Pitchumoni, Balaji Yegneswaran .World J Gastroenterol 2009 December 7; 15(45)
5.Pancreatitis in Pregnancy: a 10 year retrospective of 15 Midwest hospitals .Obstet Gynecol. 2008 November ; 112(5): 1075–1081
6. Acute pancreatitis in pregnancy: an overview .E.P. Papadakis et al. / European Journal of Obstetrics & Gynecology and Reproductive Biology 159 (2011) 261–266
7. Safety and feasibility of laparoscopic cholecystectomy during pregnancy. Mohammad1, Ibrahim A Ghaffar MD 1, Ahmad F El-Hussainy1, Mansour M Abd Alkhalik1, Mahmoud S Ahmad2, Taher Mostafa3.Journal of Arab society of Medical Research
8. ERCP for Gallstone Pancreatitis- The New England Journal of Medicine. Evan L Fogel, M.D and Stuart Sherman, M.D.