

Recurrent Pancreatitis in Pregnancy: A Review

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ABSTRACT

Background: Acute pancreatitis is a rare but dangerous surgical event that adversely affect pregnancy and worsen the both maternal and fetal outcome. The estimated incidence is 1 in 10,000 pregnancy. The diverse outcome that are responsible for the formation of abscess, pseudocysts and multiorgan dysfunction. The dual challenging problem peculiar to gravid state that have to decide a balance between risk and benefit for pregnancy continuation near term along with subsidence of acute abdomen. Among the aetiological background cholelithiasis is of prime importance as the physiological, biochemical and endocrine changes during pregnancy affect gastrointestinal and hepatobiliary system favourable for bile stasis, hyper lipidemia and calculus formation. Cholelithiasis can block the bile duct resulting in inhibition or stoppage of pancreatic enzyme travelling to small gut that regurgitate to pancreas which are irritant to pancreatic cell and initiator of inflammation of variable range e.g. from acute chronic.

Acute Biliary Pancreatitis (ABP) may also occur, a condition which is defined as acute pancreatitis (AP) associated with gall stone or sludge in the biliary tree or Gallbladder (GB).

Diversity of presentation provide diagnostic dilemma to the clinician and mimic differential diagnosis of acute abdomen specially during early pregnancy associated with hyperemesis.

Recent advancement in diagnostic and therapeutic modalities carry better prognosis in properly select cases, well set up arrangement specially to arrest Preterm Labour (PTL).

The purpose of the review is that, there have been significant developments in the diagnosis, clinical approach and management of pregnant woman with Recurrent Pancreatitis (RP) in the last decade. This review systematically summarizes the current understanding of recurrent pancreatitis.

Methodology: This current study is a review of published studies and articles by using PubMed and Google Scholar. Structured search strategy using appropriate key words and title.

Conclusion: With a focused approach and appropriate investigations, the etiology of recurrent pancreatitis can be identified in a significant proportion of pregnant woman. Therapeutic option are limited and future research is needed to improve understanding of the disease.

KEY WORDS

Pancreatitis; Pancreatic enzyme; Pregnancy.

INTRODUCTION

Recurrent acute pancreatitis is defined as more than two attacks of acute pancreatitis without any evidence of chronic pancreatitis.

Considering the underlying aetiologies are :

* Sludge or bile crystals of CBD.

* Dysfunction of Sphincter of Oddi (SOD).

* Anatomic variation of ductal system that interfere with outflow of pancreatic juice

* Obstruction of the main pancreatic duct or pancreatico biliary junction

* Alcoholism

* Occult choletithiasis

* Idiopathic

* Pregnancy.

The physiological and biochemical changes during pregnancy such as cholesterol secretion in the hepatic bile increase during 2nd and 3rd trimester compared to bile acid and phospholipids so that bile become supersaturated.¹

Endocrine changes during pregnancy i.e. hyperestrogenism and triglyceridemia with familial tendency in certain gravida triggers the pathology, that provide a sensitizer for the particular individual.²

Triglyceride (TG) level over 1000mg/dl are necessary to initiate pancreatitis but reported incidence is reducing with bowel rest including total parenteral nutrition.³

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When Triglyceride (TG) level become too high; oxygen cannot adequately travel to the pancreas via the bloodstream followed by initiation and propagation of inflammatory impulse of pancreatitis.

Metabolic changes during pregnancy such as increase or rise in lipid and lipoprotein including triglyceride specially in the 3rd trimester that may peak upto three fold which act as inducer of inflammation when serum biochemistry level remain between 750-1000mg/dl.^{4,5}

The another biochemical event in pregnancy pancreatitis is the reduction of serum calcium level leading to secondary hypocalcemia that can be overcome by slow I/V administration of calcium gluconate.⁶

Pregnancy itself is a stressful state and stress is also considered to be a risk factor for pancreatitis specially chronic one, probably by sensitizing the exocrine portion of pancreas by exerting detrimental effect through activating distinct Heat Shock Protein (HSP) including HSP 27, HSP 60, TNF α also having mediator power to provide synergistic detrimental effect.

Stress is also considered as "threatened homeostasis" that can include physical or psychological force or both. Activation of hypothalamo pituitary adrenal axis and central sympathetic outflow that resulting in visceral hypersensitivity through release of different substance e.g. substance P and calcitonin gene related peptide from afferent nerve pathway.

Recent study revealed a link between pancreatitis and transmembrane conductance regulator gene mutation.⁷

SEARCH STRATEGIES

Relevant literatures were searched during the period from January-March 2022 through PubMed and Google Scholar search engines. The key search items were "Pancreatitis; Pancreatic enzyme; Pregnancy". Filters were applied and article types selected were "Recurrent Pancreatitis in Pregnancy". Available articles published between 1972 to 2022 along with available references of those articles were reviewed.

DISCUSSION

Acute Pancreatitis In Pregnancy (APIP)

It is a challenging clinical problem though relatively limited but expanding clinical based issues.

The condition raises with gestational age i.e. 52% during 3rd trimester and 12% during 1st and 2nd trimester though the relationship between pregnancy and pancreatitis remain obscure and unclear. Observation revealed that 3rd trimester Acute Pancreatitis In Pregnancy (APIP) is associated with PE and HELLP syndrome.⁸

High level of estrogen is an inducer of increase cholesterol secretion in the hepatic bile and become supersaturated, associated progesterone secretion resulting in increase gall bladder volume, delayed emptying of bile responsible for bile stasis which offer a favourable media for calculus formation preferably in later period of gestation.⁹

Altered fluid and electrolyte balance during pregnancy resulting in weight gain that also predispose to biliary sludge and cholelithiasis.

Raised intraabdominal pressure of gravid uterus during 3rd trimester produce mechanical pressure on the biliary duct that increase the risk of Acute Pancreatitis (AP) which may aggravate even during early puerperium. The incidence is increased in this case during previous puerperium; so after that laparoscopic cholecystectomy was performed.

Reduced activity of lipoprotein lipase resulting in at least 2.5 fold increase in triglyceride level which may persist a span of six weeks predispose to women at risk of developing acute pancreatitis after pregnancy reported incidence is that, condition may decrease with bowel rest including total parenteral nutrition.¹⁰

Other aetiological background eg. alcohol abuse responsible for 10% cases. Significant alcohol intake means more than 3.5 drink daily for more than 5 years.^{11,12}

Inflammation results from upregulation of a multitude of proinflammatory signalling molecules including TNF α , IL-6, IL-8 and others.

Activation of inflammatory pathway in the pancreas, is thought to damage pancreatic tissue and accelerate the disease progression.

So the prime pathological event include : Initiation and propagation of inflammatory mediators which are responsible for inhibition of secretion and activation of intracellular protease, these are co-related with the morphological changes in the acini, such as :

- * Retention of enzyme content
- * Formation of large vacuoles having both digestive enzymes and lysosomal hydrolases that lead to necrosis.

Chemokin is released from the damaged pancreatic tissue which attract inflammatory cell and call for systemic upset response which is the determinant of the severity of the disease.¹³

Poor digestion and absorption of food specially fatty diet due to pancreatic damage resulting in weight loss and stercorrhoea (Bulky and smelly bowel movement).

The ultimate progression to the development of IDDM, stenosis or vascular obstruction of CBD, duodenum and pancreatic main duct; the ultimate development of pancreatis caroinoma.¹⁴

The final mirror image of Systemic Inflammatory Response Syndrome (SIRS) multiorgan dysfunction objectified by physiologic failure of interdependence organ system.¹⁵

The incidence of Fetal Distress (FD) and fetal loss increase with the worsening of the disease.

Once upon a time Acute Pancreatitis In Pregnancy (APIP) reported maternal and fetal mortality as high as 20% and 50% respectively.¹⁶

But recent advancement including modern diagnostic aid and available management options even endoscopy performed during conception provide better prognostic outcome.¹⁷

The rate of maternal mortality is less than 1% and the incidence of Preterm Labour (PTL) is about 20% specially pancreatitis is associated with cholelithiasis. Sometimes fetal mortality is observed in the form of miscarriage or Stillbirth (SB).¹⁸

Clinical Profile

- * Epigastric pain and tenderness of variable degree which radiates to left flank or back including muscle guard and rigidity
- * Nausea, vomiting, abdominal distension, low grade fever, tachycardia and hypotension
- * Sometimes confused with DU perforations, cholecystitis, bowel obstruction and HELLP syndrome.

Biochemical Parameter¹⁹

- * Hematological and biochemical modification may influence the test interpretation-
- * Full Blood Count (FBC)
- * Serum calcium level
- * Serum amylase level
- * Serum triglyceride level
- * Serum lipase level more than 178 u/l
- * Liver function tests
- * Viral marker are necessary to exclude HBV and HCV induced AP.

Limitation of Serum Amylase

Serum amylase level gradually increase upto 25th week of gestation; thereafter gradually decline. Biomarker more than 418 U/L are suspected but it may increase in certain disorder eg. cholelithiasis, bowel obstruction and ruptured ectopic pregnancy.

USG Evaluation

- * Time tested and consider to detect pancreatic size and duct appearance
- * To delineate peripancreatic collection.

Role of Contrast Enhanced Computed Tomography (CECT)

- * To image pancreas and surrounding structure
- * Peripancreatic inflammation
- * Distorting pancreatic contour
- * Gross ascites.

Recent Advancement in Diagnostic Profile Milestone Development

- * Endoscopic US
- * MRI
- * ERCP
- * MRCP.

Limitation of MRCP

- * Magnetic Resonance Cholangio pancreatography
- * Should be avoided during 1st trimester
- * Only diagnostic modality is available
- * To remain NBM at least for 8 hours before the procedure
- * To leave all jewellery and accessories before procedure
- * Usually offer to detect aetiology of jaundice in pancreatitis
- * To detect gallstone, narrowing, blockage or tumour of the pancreatic duct.

Limitation of ERCP

- * Diagnostic modality is to be avoided if possible due to associated risk e.g. bleeding, perforation, infection and fetal radiation.

Recent Advancement in Surgical Options and Conservative Approach

- * Endoscopic sphincterotomy
- * Biliary stenting
- * CBD stone extraction
- * Usually preferred to prevent recurrence and postpone cholecystectomy until delivery.

Definitive Approach and Role of Laparoscopy²⁰

- * Can be performed during any trimester but considering the safety profile preferred in 2nd trimester to minimize fetal and anaesthetic hazard
- * Prophylactic antithrombotic administration
- * Well set up arrangement, to minimize operating time, avoid veres needle and maintenance of proper position
- * Suggested by American Gastrointestinal and Endoscopic Surgeons (SAGES).

Role of Tocolysis

Though limited use but offer better prognostic outcome as a short term prophylaxis when administered following laparoscopy for 48-72 hours to prevent Preterm Labour (PTL), but no reported consequences seen either on mother or fetus.

Dietary Influences

- * As acute pancreatitis is a self limiting state in most instances and undergo healing
- * As pancreatitis produce dehydration, so plenty of fluid intake is mandatory throughout the day
- * Healthy diet have definite role in receiving our pancreas

- * To take or eat many small meals and snacks daily instead of three large meals; to eat between six and eight throughout the day to facilitate easy digestion
- * To avoid too much fibre at once to avoid slow digestion and reduction of enzyme effectiveness
- * To consult with dietician is necessary to learn how to change eating habits for damage.

Necessity of Fat Soluble Vitamins

People who are attacked by pancreatitis experience malnutrition; as they are found most commonly lacking in vitamin A, D, E, K as these particular agents can tax the digestive system by causing insulin level to spike.

How to Consider Regular Foods to Improve Healing or Maintain Healthy Pancreas

- * To focus on foods that are rich in protein, antioxidants and low in animal fat.²²

Importance of Herbs and Plant Sources

I. To flavour foods with herbs and spices e.g. basil, tarragon or mint, fat free sauces or lemon juice (Instead of butter)

II. Lemons : necessary to promote the release of vital digestive enzymes from pancreas

III. Limes and Kiwi fruits provide valuable role for smooth running of pancreas

IV. Haritaki: Natural remedy as well as having formidable cancer fighting properties; probably have capability to prevent cancer producing cell in pancreas by apoptosis. Oral intake lowers blood sugar levels by 43.2% in diabetic individual

V. Oregano: Animal studies revealed that having power to reduce pancreatic amylase and antihyperglycemic property to prevent long term consequence of DM

VI. Olive leaves: Oleic acid content that are capable of providing antiinflammatory property observed in pancreatitis

VII. Garlic: Stimulator for manufacturing ample level of insulin

VIII. Turmeric: Content curcumin is a naturally occurring substance present in the root of curcuma longa that provide distinctive yellow colour of the curry dishes. Rat model study of pancreatitis noticed that curcumin decrease the level of several marker that are typical for the diagnosis of the disease. Such as: Serum lipase and amylase concentration, neutrophil accumulation and trypsin activation. Inhibition of Reactive Oxygen Species (ROS).

As a nontoxic, naturally occurring product necessary for augmentation of beneficial effect to prevent and treat pancreatitis

XI. Ginger: Animal study on diabetic rat revealed that to provide protection of pancreatic tissue from lipid peroxidation and prevention of tissue damage offered by its antioxidant property

X. Caffeine: University of Liverpool observed that limited intake of caffeine can reduce the risk of alcohol induced pancreatitis through partially closed special channel within the cell.

XI. Cedar berries: Fruits are beneficial to improve digestive function of the pancreas and maintain normal pancreatic operation including blood sugar stabilisation.

Choice of Fish

- * Those contain omega-3 fatty acids which may prevent recurrent hypertriglyceridemia during pregnancy. Such as: Salmon, lake trout, tuna and herring.

Selection of Meat

- * To select lean meat, cut off all the visible fat
- * Chicken and turkey without skin.

Dietary Plan as to Maintain Natural Detoxification Process

I. To drink plenty of water

II. To eat plenty of vegetables and fruits eg. mango, berries etc

III. To maintain regular bowel movement through intake of high fibres

IV. To take fat free icecream, cream cheese or yogurt

V. To eat low fat icecream, frozen yogurt or sorbet (Frozen desert).

Selected Best Food for Pancreas

These are necessary for protection of the pancreas from damage, eg. Cruciferous vegetables, lemon, oregano, dandelion, garlic and tofu.

Antioxidant rich foods eg. dark leafy vegetables, red and blue berries, sweet potatoes, grapes, carrots walnut.

Strictly Prohibited Food, so Should be Avoided Affected by Pancreatitis²³

I. Red meat, organ meat, bake broil organ meat

II. Fried foods e.g. fries and potato chips

III. Mayonnaise, margarine and butter

IV. Full fat dairy

V. Pastries and dessert with added sugar

VI. Canned fish eg. Sardins in olive oil

VII. Fried fish in fat or butter.

Management Paradigm²⁴

I. Immediate hospitalization for prompt assesment, observation with close maternal and fetal monitoring Preferred in:

- * During acute phase

- * Usually undergo spontaneous healing

- * As a self limiting disorder usually respond in most instances.

II. Pancreatic pseudocyst formation:

- * Observed in CT in 5% cases
- * Usually undergo resolution in 30-40% case.

III. To reduce serum TG level:

- * Lipoprotein apheresis and plasmapheresis are known to reduce serum triglyceride level.

IV. Life threatening issues may be required in 5% cases eg.

- * Necrosis
- * Multiorgan failure that include : CVS, Pulmonary and Renal System
- * To consider for ICU admission and Multidisciplinary Team (MDT) approach.

LIMITATION

It is a small study, so the focal points of this study might not be representative of the actual scenario.

CONCLUSION

- * Diagnosis of exclusion is mandatory to decide for management schedule as till date no protocol is recommended though conservative approach is followed.
- * Being a small organ pancreas is often ignored but regarding digestive and endocrinology provide vital function.
- * Life style and dietary modification can provide better option to reduce severity and prevent recurrence.
- * Health care professional should be familiar with the pregnancy physiology and due consideration with the pathology accordingly.

RECOMMENDATION

The focal points of observation from this study might be taken into consideration for future planning.

DISCLOSURE

The author declared no competing interest.

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