Acute Pancreatitis in Children

Acute pancreatitis represents a diagnostic challenge in the pediatric age group. Although it occurs less frequently in children than in adults it is probably more common in childhood than has previously been appreciated and may have significant morbidity and mortality. It has numerous causes, an obscure pathogenesis, few effective remedies, and sometimes an unpredictable outcome.

Although the majority of adult cases of acute pancreatitis can be attributed to either alcohol or gallstone disease, the causes of acute pancreatitis in childhood are more numerous and include trauma, infection medications, anatomic variants and systemic metabolic disorders.

Classification

The original clinical classification of pancreatic inflammation, established at the Marseilles symposium in 1963, comprised acute pancreatitis, relapsing acute, chronic relapsing and chronic pancreatitis (1). Acute pancreatitis was characterized by clinical and pathologic reversibility, whereas chronic pancreatitis was characterized by permanent morphologic changes in the pancreas. Neither etiology nor severity was included in the classification, and it often proved difficult to clinically distinguish between the relapsing acute and chronic relapsing categories. The classification was redefined at the Second International Symposium in Marseille in 1984. Both these intermediate categories were eliminated and pancreatitis was as acute or chronic pancreatitis (2).

In Atlanta in 1992, a clinically based classification system for acute pancreatitis was proposed. According to this group, acute pancreatitis is defined as an acute inflammatory process of the pancreas, with variable involvement of the peri-pancreatic tissues or remote organ systems. Illness severity is assessed using the APACHE II system (3) or Ranson Criteria (4) and also information is obtained by contrast enhanced computerised tomography (CT) regarding the extent of the injury, and the process is divided into mild and severe forms. This system allows for reclassification of the patients diagnosis based on additional information obtained during hospitalization (5).

Pathogenesis

The primary initiating event, whether traumatic, infections or metabolic, is damage to the pancreatic, acinar cell by premature activation of digestive enzymes within the cell. The damaged acinar cell then attracts inflammatory cells and activates platelets and the complement system, which leads to the release of cytokines (such as tumor necrosis factor alpha, interleukin, nitric oxide and platelet activating factor), free radicals, and other vasoactive substances. These substances damage the gland directly causing pancreatic edema, ischaemic necrosis, and eventual loss of glandular tissue.
It remains unclear what constitutes the primary event leading to intrapancreatic proteolytic enzyme activation. Most speculation has entered around two hypotheses: (1) Reflux of duodenal contents into the pancreatic duct, where enterokinase may activate trypsinogen or (2) pancreatic ductal hypertension, resulting from continued secretion into an obstructed duct leading to rupture of small ducts, extravasation of juices into the gland, and subsequent intraparenchymal activation of enzymes. Recent findings cast doubt on this concept and propose that enzymes become activated by lysosomal hydrolases within the pancreatic acinar cell itself. (6).
Several studies have shown that oxygen free radicals play an important role in the development of inflammation in acute pancreatitis (7, 8)
Two additional factors suggested as potentially contributing to the pathogenesis of pancreatitis include abnormalities in pancreatic microcirculation with resultant ischemia (9, 10) and emotional cases (11).

**Etiologies**

There is a wide variety of causes of acute pancreatitis in the pediatric age group. In adults, biliary tract disease and alcoholism are two commonest causes. In contrast, the causes of acute pancreatitis in childhood are quite different, and the commonest etiologic factors are trauma, multisystem disease, and drugs (12, 13, 14).

Multisystem disease includes patients with a wide varieties of systemic conditions or disorders affecting multiple organs, such as sepsis, shock, systemic infections, collagen-vascular disease, inflammatory, bowel disease, and Reye's syndrome. In recent years more patients with acute pancreatitis in association with kawasaki disease, hemolytic uraemic syndrome and Henoch schonlein purpura have been reported. Viral infections, congenital structural anomalies and metabolic diseases are also considered as common causes of acute pancreatitis in childhood. In a large number of cases, no particular cause is identified.

Infections could result from measles, mumps, epstein-barr virus, coxsackie B, rubella, hepatitis A and B, influenza, echovirus, mycoplasma, typhoid, malaria, ascaris lumbricoides (leads to duct obstruction).

As for congenital pancreatic anomalies, the commonest and most controversial entity has been pancreas divisum (dominant dorsal duct syndrome). Pancreas divisum occurs when the dorsal and ventral pancreatic ducts fail to fuse during embryogenesis. As a result, most of the pancreatic parenchyma is drained by the dorsal duct, with a relative obstruction to flow. Most experts consider this anatomic variant to be a significant cause of relapsing pancreatitis that should be treated by papillotomy (15). However, other authors consider pancreas divisum a normal anatomic variant that is, at most, an infrequent cause of pancreatic pain.

In a large number of cases no particular cause is identified. A detailed list of causes is given in table:-

- **Trauma**
  - Abdominal trauma
  - Child abuse
  - Burns
  - Surgical trauma

- **Systemic Disease**
  - Infections
  - Sepsis
  - Shock
- Collagen vascular disease
- Henoch Schonlein purpura
- DVS
- Kawasaki disease
- Inflammatory Bowel Disease
- Reye's Syndrome

**Drugs**
- Chlorthalidone
- L-Asparaginase
- Azathioprine
- 6-Mercaptopurine
- Sulfonamides
- Sulfasalazine
- Nitrofurantoin
- Furosemide
- Metronidazole
- Estrogens
- Tetracycline
- Volproic acid
- Corticosteroids
- NSAIDS
- Metyldopa
- Mrenfornun
- Procainamide
- Iatrogenic hypercalcemia

**Toxin**
- Ethyl alcohol
- Methyl alcohol
- Heroin
- Amphetamines
- Organophosphate insecticides
- Acetaminophen
- Yellow Scorpion bite

**Metabolic Disorders**
- Diabetes mellitus
- Hyperlipidemia (Type I, IV, & V)
- Hyper parathyroidism
- Wilson's disease
- Renal failure
- Hypercalcemia
- Hyperlipidemia
- Uremia
- Alpha 1 - antitrypsin deficiency
**Pancreatic Disorders**
- Cystic fibrosis
- Diarrhoea
- Pancreatic divisum
- Duplication
- Abnormalities of duct

**Biliary Disorders**
- Gall Stone
- Choledochal cyst
- Biliary tree anomalies
- Duodenal obstruction
- Parasites
- After endoscopic retrograde cholangiopancreatography (ERCP)

**Gastro Intestine disorders**
- Duodenal ulcer, penetrating
- Duplications

**Transplantation**
- Renal transplantation
- Graft-versus-host disease

**Miscellaneous**
- Hereditary
- Idiopathic
- Postoperative

**Author's Experience:-**

**Table - 2 Causes of Acute Pancreatitis in 272 children**

<table>
<thead>
<tr>
<th>Cause</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic causes</td>
<td>22</td>
</tr>
<tr>
<td>Trauma</td>
<td>20</td>
</tr>
<tr>
<td>Infections</td>
<td>15</td>
</tr>
<tr>
<td>Biliary tract disease</td>
<td>14</td>
</tr>
<tr>
<td>Drugs</td>
<td>13</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>11</td>
</tr>
<tr>
<td>Congenital anomalies</td>
<td>5</td>
</tr>
</tbody>
</table>

Data from references 17, 49, 62, 139, 159 and 154
Table - 3 Medications & toxins associated with pancreatitis

<table>
<thead>
<tr>
<th>Acetaminophen overdose</th>
<th>Diphenoxylate</th>
<th>Organophosphates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>Didanosine</td>
<td>Penicillin</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>Enalapril</td>
<td>Pentamidine</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>Erythromycin</td>
<td>Phenformin</td>
</tr>
<tr>
<td>L-Asparaginase</td>
<td>Estrogen</td>
<td>Piroxicam</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>Ethacrynic acid</td>
<td>Procainamide</td>
</tr>
<tr>
<td>Boric acid</td>
<td>Furadantin</td>
<td>Propoxyphene</td>
</tr>
<tr>
<td>Calcium</td>
<td>Furosemide</td>
<td>Propylthiouracil</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Heroin</td>
<td>Ranitidine</td>
</tr>
<tr>
<td>Cimetidine</td>
<td>Histamine</td>
<td>Rifampin</td>
</tr>
<tr>
<td>Chlorthalidone</td>
<td>Indomethacin</td>
<td>Salicylates</td>
</tr>
<tr>
<td>Cholestyramine</td>
<td>Isoniazid</td>
<td>Sulfasalazine</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>Meprobamate</td>
<td>Sulfonamides</td>
</tr>
<tr>
<td>Clonidine</td>
<td>6-Mercaptopurine</td>
<td>Sulindac</td>
</tr>
<tr>
<td>Cytarabine</td>
<td>Mesalamine</td>
<td>Tetracycline</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Methotrexate</td>
<td>Thiazides</td>
</tr>
<tr>
<td>Cyproheptadine</td>
<td>Methyldopa</td>
<td>Trimethoprim-sulfamethoxazole</td>
</tr>
<tr>
<td>Cyproheptadine</td>
<td>Metronidazole</td>
<td>Valproic acid</td>
</tr>
<tr>
<td>Cytosine arabinoside</td>
<td>Nonsteroidal anti-inflammatory drug</td>
<td>Vincristine</td>
</tr>
<tr>
<td>Diazoxide</td>
<td>Nitrofurantoin</td>
<td>Venom (scorpion, spider)</td>
</tr>
<tr>
<td>Dideoxycytidine</td>
<td>Opiates</td>
<td>Vitamin D</td>
</tr>
<tr>
<td></td>
<td>Oxyphenbutazone</td>
<td></td>
</tr>
</tbody>
</table>

Clinical Spectrum

Acute pancreatitis can present with a wide spectrum of symptoms and complications (16, 17); the clinical course is presently unpredictable. The diagnosis is difficult to establish unless a high index of suspicion is maintained. A combination of clinical signs and symptoms, in concert with supportive biochemical abnormalities and imaging techniques, is usually necessary to provide a certain diagnosis.

Table - 4 The important clinical features of Acute pancreatitis are as follows:

Symptoms
- Abdominal Pain
- Anorexia
- Nausea
- Vomiting
- Coma (rare)
- Dyspnea (rare)
**Signs**
- Localized epigastric tenderness
- Abdominal wall rigidity
- Rebound tenderness
- Abdominal distention
- Diminished or absent bowel sounds
- Hypotension or shock
- Low-grade fever
- Pleural effusion
- Asites
- Oliguria/anuria
- Respiratory distress
- Grey - Turner sign
- Cullen's sign
- Bluish discoloration of flanks
- Bluish discoloration of periumblical area

Abdominal pain, as in adults, is the outstanding symptom, but on rare occasions pain may be absent especially in younger patients. Typically the pain is sudden in onset increase gradually in severity and reaches maximal intensity after a few hours. It is located most commonly in the epigastrium other sites include right upper quadrant, periumblical area, back or lower chest and occasionally patients complain of diffuse pain over the abdomen. Quality of pain is usually difficult to determine radiation of the pain is less frequent in children than adults and is seen in approximately 30% of cases. Pain could radiate to back, middle/lower part of abdomen, right upper quadrant and the anterior aspect of chest wall. Eating usually triggers a worsening of pain and vomiting. The patient may experience some pain relief when the knees are drawn up to a flexed trunks. The emesis may be bilious. Fever, if present, is usually low grade (35.5°C). A family history of pancreatitis should prompt the clinician to ask about symptoms of hereditary and systemic/metabolic disorders, such as diarrhea, vasculitis, joint pain, rashes, and pulmonary disease. Pain was associated with vomiting in 70% of the cases. On examination, there may be localized (epigastric) or diffuse tenderness of abdomen; rebound tenderness and guarding may be present and is usually localized to the epigastrium or upper abdomen.

Abdominal distention may be observed. In severe cases of hemorrhagic or necrotizing disease, Grey turner's sign (blue discoloration around the umblicus) Dr. Cullen's sign (bluish discoloration around the flanks) may be noted. Both signs are due to ecchymosis with entrance of blood into the fascial planes and are not pathognomonic of acute pancreatitis Hypotension or circulatoty shock or coma may be seen in patients with severe pancreatitis. Other less common findings may include pleural effusion, respiratory distress, abdominal ascites, icterus, abdominal mass malena and hematemesis.
Complications of Acute Pancreatitis

Systemic Complications
- Hypocalcemia
- Hyperglycemia
- Hyperlipidemia
- Acidosis
- Hyperkalemia

Organ System Complications
- Circulatory failure
- Renal failure
- Respiratory failure
- Gastrointestinal
- Hematologic
- Neurologic (psychosis or coma)
- Hepatobiliary

Diagnosis

There is no single diagnostic test of acute pancreatitis. The clinical diagnosis rests on a gestalt of quite variable nonspecific clinical finding, supportive laboratory tests, and imaging techniques. Occasionally the diagnosis is made with certainly at laprotomy or at biopsy. A careful history is required to determine the presence of any etiologic factors, such as a family history, associated inherited or acquired conditions, medications and trauma, previous history of unexplained episodes of pain, if any, should also be looked into.

Laboratory Investigations

Nonspecific laboratory tests

Leukocytosis with bandemia, leuко concentration, hyperglycemia, hypocalcemia, and elevated alkaline phosphatase, aspartate amino transferase and total bilirubin are frequent findings. Other nonspecific laboratory abnormalities include metabolic alkalosis, albuminuria, glycosuria, and coagulopathies. Hypoxemia with hypoalbuminemia, hypocalcemia, and azotemia with elevated glucose and lactate dehydrogenase levels reflect more progressive disease and hemorrhagic pancreatic damage.

Specific laboratory tests

The lack of a "gold standard" diagnostic test for acute pancreatitis creates substantial problems in clinical practice, and in interpretation published report. The available laboratory tests and imaging techniques are summarized in Table- 5
Table - 5:-

<table>
<thead>
<tr>
<th>Laboratory Tests</th>
<th>Imaging Techniques</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum amylase</td>
<td>Plain film of abdomen</td>
</tr>
<tr>
<td>Urine amylase</td>
<td>Plain film of chest</td>
</tr>
<tr>
<td>Amylase creatinine clearance ratio</td>
<td>Upper gastrointestinal barium</td>
</tr>
<tr>
<td>Amylase isoenzymes</td>
<td>Pancreatic ultrasonography</td>
</tr>
<tr>
<td>Serum lipase</td>
<td>Abdominal computed tomography</td>
</tr>
<tr>
<td>Serum proteases</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>Serum ribonuclease</td>
<td>Endoscopic retrograde cholangiopancreatography</td>
</tr>
</tbody>
</table>

Serum Amylase

Although it has a relatively low sensitivity and specificity (75% - 92% and 20% - 60% respectively) serum amylase remains the most frequently utilized biochemical test for acute pancreatitis, its serum level rises within 2 to 12 hours, and in uncomplicated cases, remains elevated for 2-5 days. A protracted elevation raises the suspicion of a pseudocyst or macroamylasemia. Serum amylase levels greater than three times normal are considered significant for the diagnosis. Because amylase is cleared by the kidneys, elevated urinary amylase levels may exist 24 hours after normalization of serum levels. The level of serum amylase bears no relationship with the severity of pancreatitis or its clinical course. Although serial determination with a gradual decline usually can indicate improvement, clinical deterioration can parallel amylase level normalization. The sensitivity of amylase in pediatric acute pancreatitis is less than in adults.

Lipemia may interfere with amylase determination, (18) and total acinar destruction may result in normal serum amylase during acute pancreatitis. It is also well known that there are many nonpancreatic causes of hyper amylasemia (as show in table) By raising the cut off level from three to six times the upper limit of normal, specificity increases for pancreatitis, but at the expense of sensitivity.

Table - 6 - Conditions associated with Elevated Serum Amylase

<table>
<thead>
<tr>
<th>Pancreatic</th>
<th>Salivary</th>
<th>Both (or unknown)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic aneurysm -abdominal</td>
<td>Anorexia</td>
<td>Alcoholism</td>
</tr>
<tr>
<td>Appendicitis</td>
<td>Bulimia</td>
<td>Burns</td>
</tr>
<tr>
<td>Biliary duct obstruction</td>
<td>Infection (mumps)</td>
<td>Cirrhosis</td>
</tr>
<tr>
<td>Biliary tract disease</td>
<td>Lung cancer</td>
<td>Cystic fibrosis</td>
</tr>
<tr>
<td>Choledocholithias</td>
<td>Ovarian tumor /cyst</td>
<td>Diabetic ketoacidosis</td>
</tr>
<tr>
<td>Endoscopic retrograde, cholangiopancreatography</td>
<td>Parotitis</td>
<td>Drugs</td>
</tr>
<tr>
<td>Intestinal infarction, obstruction, or perforation</td>
<td>Pneumonia</td>
<td>Head trauma</td>
</tr>
<tr>
<td>Pancreatic duct obstruction</td>
<td>Salivary duct obstruction</td>
<td>Hepatitis</td>
</tr>
<tr>
<td>Pancreatic tumors</td>
<td>Salpingitis</td>
<td>Heroin addiction</td>
</tr>
<tr>
<td></td>
<td>Trauma</td>
<td>Opiates</td>
</tr>
</tbody>
</table>
Amylase Isoenzymes

Normally, 60% of serum amylase is salivary and the rest is pancreatic. Although in acute pancreatitis, the majority of serum amylase is of pancreatic origin, other abdominal conditions also increase pancreatic isoamylase. Fractionation of isoamylase isoenzymes to pancreatic amylase is more discriminatory than amylase levels, but not superior to lipase assay.

Amylase Creatinine clearance ratio

The higher ratio in pancreatitis is due to increased renal clearance of amylase in relation to creatinine due to decreased renal tubular reabsorption of amylase in acute pancreatitis. Subsequently, this test is not specific, and in many other conditions of hyperamylasemia, the ratio is high. It is agreed that the clearance ratio does not add any important diagnostic information to that provided by serum amylase determination.

Serum Lipase

Serum lipase levels have a reported clinical sensitivity of 86% to 100% and clinical specificity of 50% to 99%. By increasing the cut-off level to greater than three times the upper limit of normal, sensitivity can be increased to 100% and specificity to 99%. Lipase levels remain elevated for a longer period of time in the plasma than do amylase levels, beginning to increase within 4 to 8 hours after systems, peaking at 24 hours, and decreasing over 8 to 14 days. It should be noted, however, that the degree of elevation of amylase and lipase in the plasma does not reflect the severity of the pancreatic disease. By using serum amylase and lipase determination together, clinical sensitivity for the diagnosis of pancreatitis increases to 94%.

Considerable controversy exists concerning lipase superiority compared with amylase determination. Lipase is also found in intestinal mucosa, stomach, adipose tissue, leukocytes, and breast milk and can be elevated in the serum of patients with other abdominal conditions.

Serum Immunoreactive Trypsin

The only source of trypsin in the human body is the pancreas. Total immunoreactive trypsin increases in acute pancreatitis earlier as compared with amylase. Its sensitivity is higher than lipase and pancreatic isoamylase with similar specificity and correlates with disease severity. Unfortunately, it's not readily available in most centres.
Ribonulcease

The concentration of serum ribonuclease is low in serum, and pancreatic ribonuclease can be distinguished immunologically from other sources of ribonulcease. Elevated pancreatic ribonuclease levels in serum have been suggested to be indicative of pancreatic necrosis (23).

Imaging Procedures

The most useful and frequently used imaging procedure in evaluating acute pancreatitis are abdominal ultrasonography and CT Scan.

Conventional radiology

It’s of limited value in evaluating acute pancreatitis. However a plain film of abdomen and chest are done to rule out local complications and other abdominal catastrophes such as a perforated viscus or appendicolith suggesting acute pancreatitis. The findings are summarized in table - 7.

<table>
<thead>
<tr>
<th>Chest Radiograph</th>
<th>Abdominal Plain Film</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelike atelectasis</td>
<td>Regional small bowel ileus (sentinel loop)</td>
</tr>
<tr>
<td>Basilar infiltrates</td>
<td>Dilatation of transverse colon (colon cut-off sign)</td>
</tr>
<tr>
<td>Elevation(s) of hemidiaphragm(s)</td>
<td>Absence of air in descending colon</td>
</tr>
<tr>
<td>Left pleural effusion</td>
<td>Generalized ileus</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>Blurring of the left psoas margin</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>Pancreatic califications</td>
</tr>
<tr>
<td></td>
<td>Diffuse abdominal haziness</td>
</tr>
<tr>
<td></td>
<td>Peripancreatic extraluminal gas bubbles</td>
</tr>
<tr>
<td></td>
<td>Pancreatic pseudocyst</td>
</tr>
</tbody>
</table>

Accumulation of fluid within the pleural space is indicative of severe pancreatitis since high concentrations of amylase are generally present within pleural collections, this measurement can be helpful in confirming the diagnosis in difficult case.

Contrast studies of upper gastric intestinal tract rarely provide useful information. The duodenal loop may appear widened and the inverted 3 appearance (Frostberg sign), with the middle apex of 3 being the origin of the duct and the curves of the 3 indicating swelling of the pancreatic head. The stomach may be displaced forward or medially by retroperitoneal swelling or a pseudocyst. Barium enema examination may show extrinsic compression and/or displacement of the midtransverse colon.
Ultrasonography

Abdominal ultrasound is the most frequently used and useful imaging investigation performed in patients with suspected acute pancreatitis. The two major sonographic findings are increased pancreatic size and decreased pancreatic echogenicity. (21,24). The echogenicity marker seems to be more reliable than pancreatic size alterations. In "normal" children, the pancreatic echodensity is equal to that of the left lobe of the liver. In children, sonography has a positive predictive value of 0.93 and negative one of 0.78 in acute pancreatitis. (24) Hypoechoogenicity was reported in 44% of incidences of acute pancreatitis in children.

Overlying gas due to ileus may present a technical problem but water can be given to fill the stomach and act as an acoustic window.

Beside size, contour and echogenicity, sonography can provide information on pancreatic duct, any calcification, pseudocyst, fluid in abdomen and pleural space.

Abdominal Computed Tomography

Abdominal computed tomography is usually reserved for situations where sonography is technically unsatisfactory or where better anatomic definition is required. Contrast-enhanced CT is the imaging method of choice in delineating the pancreas, evaluating the severity of and detecting the complications of acute pancreatitis. In mild pancreatitis, the CT scan demonstrates a normal pancreas in 15% to 30% of patients. (25). In more severe instances, however, nearly always the scan is abnormal. Computed tonographic scan signs include changes in size and texture of the inflamed pancreas, pseudocysts, abscesses, calcifications, duct enlargement, peripancreatic edema, peritoneal exudate, and bowel distention. (25, 26). Dynamic CT pancreatography, in which large doses of intravenous contrast medium are given rapidly and the pancreas is analyzed by thin tomographic cuts, is now used to identify pancreatic perfusion defects that correlate with pancreatic necrosis. (27)

Endoscopic Retrograde Cholangiopancreatography

With the development of a smaller pediatric side-viewing endoscopy, endoscopic retrograde cholangiopancreatography examination can be successfully performed in small children. In acute pancreatitis, the pediatric indications are evaluation of post-traumatic or postpancreatitis complications, detection of anatomic abnormalities associated with acute pancreatitis, and study of the pancreatic ducts in chronic relapsing pancreatitis or hereditary pancreatitis (28, 29). In the largest series done, mild pancreatitis was reported after the procedure in 12% of children, but in all it was self-limited. (28). In the most recent report, only 5% of children developed transient pancreatitis owing to the test (29). Endoscopy, nowadays is also used for therapeutic drainage of pseudocyst (resulting as a complication of acute pancreatitis). The cyst is
drained into the stomach or occasionally into the duodenum, depending on the site of maximum bulge of the cyst. Endoultrasound, may be used as a guide prior to this procedure.

**Clinical course and complications**

There is considerable variation in the clinical course of acute pancreatitis (30, 16). The patient may have a mild illness, appearing only moderately ill with transient abdominal discomfort, or there may be a fulminating, rapidly progressive course, with the patient developing severe pain, renal failure, circulatory collapse, and a fatal outcome within hours or days. There are no accurate data regarding mortality in children. In adults, the overall mortality rate per attack is estimated to be approximately 9%, but in severe, hemorrhagic pancreatitis the mortality is higher, ranging from 15% to 50% in large case reports (30, 31). However severe pancreatitis and associated mortality is much less in children. Clinical symptoms associated with a poor prognosis include the presence of shock, renal failure, and severe hypocalcemia; these secondary complications almost certainly occur as a result of severe hemorrhagic pancreatitis. Similarly, late complications, including hemorrhage or rupture of a pancreatic pseudocyst or development of pancreatic abscess, carry a high mortality rate.

Attempts have been made to develop clinically useful prognostic scores of disease severity in adults with acute pancreatitis by statistically analyzing early clinical features and biochemical measurements. A prognostic scoring system has not been developed for children, and most of those established for adults cannot be applied to the younger patient. For example, in the system developed by Ranson and Pasternak, (4), prognostic factors such as age (over 55 years) and volume of fluid sequestration are not applicable to children. Since large numbers of patients are required for multivariate analysis of prognostic criteria, a useful scoring system in the pediatric age group will be difficult to establish. It must be emphasized, however, that certain clinical features of pancreatitis are clear indicators of severe disease, being frequent in patients with pancreatic hemorrhage or necrosis. These include disorders of body homeostasis, such as coma, hypotension, renal failure, pulmonary edema, shock, and hemorrhage. Similarly, laboratory indicators of severe disease include hyperglycemia, hypocalcemia, hypoxemia, hypoproteinemia, raised blood urea nitrogen, leucocytosis, and a drop in hematocrit. The quantity of necrotic tissue appears to be directly correlated with the development of systemic complications and with the risk of infection, so the use of "dynamic pancreatography" has been suggested for early identification of patients most at risk (32, 33, 34).

Acute phase proteins, fibrinogen, α1 anti proteins and C-reactive protein (CRP) have all been examined as potential indicators of disease severity. CRP is probably the more useful marker of severe acute pancreatitis. In a multicentric study from Italy on 50 patients, it was seen that patients with severe pancreatitis had serum concentration of C-reactive protein significantly higher on the 1\textsuperscript{st} day and on the 3\textsuperscript{rd} day than in patients with mild acute pancreatitis (35). Other markers which appear to be predictive of the
severity of the attack with high reliability include urinary trypsinogen activation peptide (TAP) (34) and blood levels of leucocyte elastase (PMN elastase ) (36)

**Treatment**

**Medical Therapy**

The treatment of acute pancreatitis is largely supportive, and the intensity of therapy is decided by the severity of inflammation . Several specific clinical aims are followed during the treatment like

1. Removal of the initiating offender (i.e. drugs or toxins)
2. Reducing the self-perpetuating autodigestive process in the pancreas
3. Removal of digestive enzymes or toxins from the circulation or peritoneal cavity
4. Treatment of local and systemic complications

**Removal of the initiating process**

If the underlying cause in recognized such as drugs/toxins/hypercalcemia they should be eliminated. However, frequently the autodigestive and inflammatory response within the pancreas is well advanced at the time of diagnosis.

**Interruption of autodigestion**

Various nonspecific and specific clinical measures have been proposed to achieve this objective, but the therapeutic benefit of most of the strategies has not been validated in clinical trials.

**Table: 8 - Proposed methods of interrupting autodigestion**

<table>
<thead>
<tr>
<th>Objective</th>
<th>Treatment(s)</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Putting pancreas to rest</td>
<td>Nil per os</td>
<td>Questionable</td>
</tr>
<tr>
<td></td>
<td>Nasogastric suction</td>
<td>-do-</td>
</tr>
<tr>
<td></td>
<td>Antacids</td>
<td>-do-</td>
</tr>
<tr>
<td></td>
<td>Histamine antagonists</td>
<td>-do-</td>
</tr>
<tr>
<td>Inhibition/reduction of</td>
<td>Anticholinergics</td>
<td>None</td>
</tr>
<tr>
<td>secretions</td>
<td>Glucagon</td>
<td>-do-</td>
</tr>
<tr>
<td></td>
<td>Somatostatin</td>
<td>-do-</td>
</tr>
<tr>
<td></td>
<td>Vasopressin</td>
<td>-do-</td>
</tr>
<tr>
<td></td>
<td>Hypothermia</td>
<td>-do-</td>
</tr>
<tr>
<td></td>
<td>Calcitonin</td>
<td>-do-</td>
</tr>
<tr>
<td>Cell wall stabilizers</td>
<td>Prostaglandins</td>
<td>Questionable</td>
</tr>
<tr>
<td>Inhibition of proteases</td>
<td>Aprotinin</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Epsilon -aminocaproic acid</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Leupeptin</td>
<td>Animal studies only</td>
</tr>
</tbody>
</table>
Inhibition or removal of pancreatic enzymes

Enzyme inhibitors, such as aprotinin and gabexate, given intravenously or intraperitoneally did not improve the outcome in instances of severe disease (18). Supportive measures, such as total parenteral nutrition or fresh frozen plasma, also have not proved to be effective. Antibiotic coverage to prevent septic complications using ampicillin did not change the course of acute pancreatitis (18). A recent study using imipenem was successful in reducing the incidence of pancreatic sepsis in patients with necrotizing pancreatitis (37).
References:


35. R. Pezzilli et al, Pancreatology 2001; 1: 129-199, P 3 80 abstracts
