THE ROLE OF HEMOCONCENTRATION IN PROGRESSION OF ACUTE PANCREATITIS

THESIS

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THE ROLE OF HEMOCONCENTRATION IN PROGRESSION OF ACUTE PANCREATITIS

A thesis submitted in partial fulfillment of the requirements for the degree of Master of Surgery (MS) in General Surgery of the Tribhuvan University, Nepal

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Based on the studies conducted at the Department of Surgery,
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CERTIFICATE

This is to certify that the work contained in the thesis entitled **the role of hemoconcentration in progression of acute pancreatitis** is the results of the original investigative study undertaken by Dr Mohamed Shifan in the Department of Surgery under our direct supervision and guidance.

Prof. Mahesh P. Khakurel, FRCS
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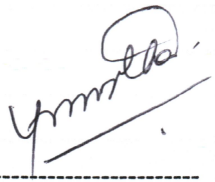
TU Teaching Hospital.



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DECLARATION

I hereby declare that this thesis work on **"the role of hemoconcentration in progression of acute pancreatitis"** has not been submitted in candidature for any degree. I will have no objection for availability of this thesis (as part or whole) for photocopy and inter-library loans for outside organization.

Dr Mohamed Shifan
MBBS

Date / /

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Mohamed Shifan.

September, 2007.

DEDICATION

For my parents, who grant me the privilege of practicing this craft and for the constant guidance and blessings the unconditional love and sacrifices they have made for my education.

For my sister, and my niece (shada) who's such a joy to be with, a great inspiration.

For my wife, for the constant support and understanding.

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ABSTRACT

BACKGROUND:

Acute pancreatitis is a complex, life-threatening disease that has many causes, few effective treatments, numerous serious complications, and an often unpredictable course. The disease may range from a mild, self-limiting inflammatory process to extensive necrosis and multi-organ failure. Despite recent advances in diagnosis and treatment, acute pancreatitis continues to be a very serious illness with an overall mortality of 5% to 10%, and the incidence of this disease appears to be rising.

Early identification of patients with acute pancreatitis who have a high risk of developing complications is of paramount importance to their management.

OBJECTIVES:

Aim of the study is to determine the role of hemoconcentration in progression of acute pancreatitis

PATIENTS AND METHODS:

It is a prospective non-randomized study conducted in 75 non-consecutive patients, over a period of one year, with the clinical diagnosis of acute pancreatitis. Ranson's scoring was done in all the patients at admission and at 48 hours. The hematocrit (Hct) which was prospectively obtained was evaluated. The course of events noted throughout hospital stay (duration of hospital stay, local or systemic complication, the need for artificial ventilation and CT scan findings noted) up to discharge of patients noted and analyzed. Hemoconcentration: was defined as a hematocrit levels more than43.0% for male and more than 39.6% for female patients.

RESULTS:

In the study undertaken in our centre described above hemoconcentration was comparable to that of ranson's score which yields the result at forty eight hours. Hence, (hemoconcentration estimation) at admission had comparable sensitivity (88.90%), specificity (94.90%), positive predictive value (84.2 %)and a higher negative predictive value (96.62%) to that of ranson's score gained after forty eight hours.

The correlation of hemoconcentration versus Ranson's score was shown significant at the 0.01 level.

Of note, Hemoconcentration does not significantly correlate with important clinical outcome variables of acute pancreatitis including organ failure and mortality rate in this study.

Its prognostic value is comparable to the more complicated Ranson's scores obtained only after 48 h. The major value of this single easily obtainable and cheap parameter on admission lies in its high negative predictive value.

KEY WORDS:

Hemoconcentration, Acute pancreatitis, Ranson's score, simplified prognostic test(s).

INTRODUCTION

More than a century after its comprehensive description by Reginald Fitz, [1] acute pancreatitis remains a common disorder with potentially devastating consequences. Although most episodes are mild and self limited, up to a fifth of patients develop a severe attack that can be fatal.[2]The overall mortality of acute pancreatitis remains 5-10 percent and may increase to 35% or higher if complications develop. [3, 4, 5]The disease's course in a patient with acute pancreatitis is not always apparent at presentation; some patients get worse before they get better. [5]

Acute pancreatitis has varied clinical manifestations, is difficult to diagnose, has an unpredictable course, and is even more difficult to prognosticate. The disease may range from a mild, self-limiting inflammatory process to extensive necrosis and multi-organ failure. [6]

Despite recent advances in diagnosis and treatment, acute pancreatitis continues to be a very serious illness with an overall mortality of 5% to 10% (Banks, 1997), and the incidence of this disease appears to be rising (Steinberg &Tanner, 1994).
Early identification of patients with acute pancreatitis who have a high risk of developing complications is of paramount importance to their management (Dominquez-Munoz et al., 1993.)

The assessment of the severity of acute pancreatitis is a critical early step in its management, as severity of acute pancreatitis predicts prognosis. A range of options are available for assessment of severity in acute pancreatitis, including clinical evaluation, standardized prognostic criteria, computed tomography (CT), and biochemical markers. Clinical assessment has limited accuracy for predicting severity early in the course of acute pancreatitis. Therefore, additional assessment using biochemical and radiologic criteria in combination with standardized criteria is appropriate to determine severity and prognosis in acute pancreatitis; a strategy emphasizing daily assessment of severity should be used.

The APACHE II (Acute Physiology and Chronic Health Evaluation) is the scoring system of choice for evaluating severity in acute pancreatitis, although it remains an imperfect tool. Computed tomographic grading of acute pancreatitis and the development of the CT severity index allow for heightened accuracy in the prediction of severity.
C-reactive protein is the standard for serum marker assessment of severity and prognosis in acute pancreatitis; other markers, including interleukin-6, polymorphonuclear elastase, and trypsinogen activation peptide, hold promise.

Acute pancreatitis is an acute inflammatory process of the pancreas that can involve peripancreatic tissues or remote organ systems, or both. [6] It may occur as an isolated attack or recur in distinct episodes with reversion to normal histology between attacks. By definition, acute pancreatitis is reversible; it is distinguished from chronic pancreatitis by the absence of continuing inflammation, irreversible structural changes, and permanent impairment of exocrine and endocrine pancreatic function. As the diagnosis of acute pancreatitis is usually made on clinical grounds and pancreatic tissue is rarely available, it can be difficult to distinguish between acute and chronic pancreatitis in the individual case.

The most commonly used classification system for acute pancreatitis distinguishes between mild and severe disease.[6] Severe disease is characterized by organ failure or local complications such as necrosis, pseudocysts, or fistulae. Scoring systems use prognostic signs to stratify patients and help in early recognition of patients with a high probability of developing severe pancreatitis

Even though the diagnosis of acute pancreatitis has become easier by the measurement of specific pancreatic enzymes, early assessment of the prognosis still remains a clinical challenge at an early stage of the disease. The imaging procedures and the elevated mediators are not widely available at the beginning. Several complex scoring systems are being used for pancreatitis. Studies that associate the hemoconcentration with the development of severe pancreatitis are present in literature.

REVIEW OF LITERATURE

Acute pancreatitis is a group of reversible lesions characterized by inflammation of the pancrease ranging in severity from edema and fat necrosis to parenchymal necrosis with severe hemorrhage. Acute pancreatitis is relatively common.

Historical note:

History offers numerous accounts of diseases that might have been acute pancreatitis. An early example being the fatal illness of Alexander the great (323 B.C). [7] The first systematic analysis of the condition emerged 2200 year later with Reginald Huber Fitz (1843-1913). In his land mark paper on acute pancreatitis published in the Boston medical and surgical journal in 1889, Fitz presented detailed clinical characteristics of 53 patients, distinguishing between hemorrhagic, suppurative and gangrenous form of the disease. [8]

However it was Chiari who in 1896 postulated that the underlying pathophysiological mechanism of the disease was pancreatic auto digestion that's the pancrease "succumbs to its own digestive properties". [9]

But it was not until Eugine Lidsay Opie (1873-1971) begetter of "common channel" hypothesis, on the basis of observation proposed that a gall stone lodged in the ampulla might occlude both the common bile duct and the pancreatic duct, so forms a common channel that would allow reflux of bile into the pancreatic duct with activation of pancreatic enzymes. [10]

Lerch *et al* have demonstrated that obstruction of the pancreatic duct alone causes necrotizing pancreatitis indistinguishable from that seen when the bile duct is simultaneously occluded[6]. Commenting on the demise of the Opie theory, Fitzgerald remarked "never in medical history have so many owed so much to a single stone". [11]

Lord Moynihan characterized the disease in 1925, "acute pancreatitis is the most terrible of all calamities that occur in connection with the abdominal viscera. The suddenness of the onset, the illimitable agony which occurs accompanies it, and mortality attendant upon it, all render it the most formidable of catastrophies". [12] Moynihan's chief contribution was to sum up the indications and detailed procedures for surgical management. [13] The 1930's witnessed a change of approach, after recognition that the mortality rate for such surgery was as high as 50-78%. A review of the time concluded, "A 10 minutes surgical discussion of acute pancreatitis should probably include 9 minutes of silence .[14]Until 1970's conservative management then prevailed.

Today we benefit hugely from contributions of Beger and Bradley among others who have characterized in detail the types of pancreatic necrosis (infected versus sterile) that do best with surgical intervention and have described the various techniques of drainage (open versus closed) [15, 16]. Nevertheless, many issues surrounding the surgical treatment remain unresolved.

Incidence:

The incidence of acute pancreatitis ranges between 5 and 80 per 100,000 populations, with the highest incidence recorded in the United States and Finland. [17] Annual incidence in the United States is 18 per 100,000 population. In a European cross-sectional study, incidence of acute pancreatitis increased from 12.4 to 15.9 per 100,000 annually from 1985 to 1995; however, mortality remained stable as a result of better outcomes.[18] Another study showed a lower incidence of 9.8 per 100,000 but a similar worsening trend over time. [19]

Anatomy

In spite of the apparent accessibility of the pancreas, several anatomic relations combine to make its surgical removal difficult. In 1898, Halsted was the first to successfully remove the head of the pancreas and a portion of the duodenum for ampullary cancer. The pancreas lies transversely in the retroperitoneal space, between the duodenum on the right and the spleen on the left. It is related anteriorly to the omental bursa above, the greater sac below, and the transverse mesocolon. For all practical purposes, it is a fixed organ.[20]

Head

The head of the pancreas is flattened and has an anterior and a posterior surface. The anterior surface is adjacent to the pylorus and the transverse colon. The anterior pancreaticoduodenal arcade can be seen on the ventral surface of the head of the pancreas, coursing roughly parallel to the duodenal curvature.[21]

The posterior pancreaticoduodenal vascular arcade is a major entity on the posterior surface of the head. This surface of the pancreatic head is close to the hilum and medial border of the right kidney, the right renal vessels and the inferior vena cava, the right crus of the diaphragm, and the right gonadal vein. [22]

The head of the pancreas may be related to the third part of the common bile duct (CBD) in a variety of ways and shows the most frequent conditions: the bile duct is partially covered by a tongue of pancreatic tissue (44%). The duct is uncovered on the posterior

surface of the pancreas in 16.5% of cases. In 9% of cases, the third part of the CBD is covered by two tongues of pancreatic tissue.[22]

Uncinate Process

An extension of the head of the pancreas (which is variable in size and shape) passes downward and slightly to the left from the principal part of the head. It further continues behind the superior mesenteric vessels and in front of the aorta and inferior vena cava. In sagittal section, the uncinate process lies between the aorta and the superior mesenteric artery (SMA), with the left renal vein above and the duodenum below. If the junction of the superior mesenteric and portal vein is low, the anterior surface of the uncinate process is related to the superior mesenteric vessels and the portal vein. [23]

- Division at the neck is equivalent to a 60% to 70% resection.
- Division at the proximal body to the left of the portal vein above and to the superior mesenteric vein below is a 50% to 60% resection.
- Even with an 80% pancreatectomy, good exocrine and endocrine activity are present.

Neck

The neck of the pancreas can be defined as the site of passage of the superior mesenteric

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Neck

The neck of the pancreas can be defined as the site of passage of the superior mesenteric vessels and the beginning of the portal vein dorsal to the pancreas. This pancreatic segment is 1.5 to 2.0 cm long, and it is partially covered anteriorly by the pylorus. The gastroduodenal artery passes to the right of the neck and provides origin for the anterior superior pancreaticoduodenal (ASPD) artery. Posterior to the neck, the portal vein is formed by the confluence of the superior mesenteric and splenic veins. Near the inferior margin of the pancreatic neck, one can often see the terminations of the inferior pancreaticoduodenal vein and right gastroepiploic vein where they drain into the superior mesenteric or splenic veins or into the portal vein proper. [23]

Body

The anterior surface of the body of the pancreas is covered by the double layer of peritoneum of the omental bursa that separates the stomach from the pancreas. The omental tuberosity (tuber omentale), a blunt upward projection of peritoneum from the body, contacts the lesser curvature of the stomach at the attachment of the lesser omentum. The body is also related to the transverse mesocolon, which divides into two leaves: the superior leaf covers the anterior surface and the inferior leaf passes inferior to the pancreas. The middle colic artery emerges from beneath the pancreas to travel between the leaves of the mesocolon. [24]

Posteriorly, the body is related to the aorta, the origin of the SMA, the left crus of the diaphragm, the left kidney and its vessels, the left adrenal gland, and the splenic vein. Small vessels from the pancreas enter this vein. They must be ligated during pancreatectomy if the splenic vein and the spleen are to be preserved. [24]

Tail

The tail of the pancreas is relatively mobile; its tip reaches the hilum of the spleen in 50% of the cases, lies above the hilum in 8%, and below in 42%. Together with the splenic artery and the origin of the splenic vein, the tail is contained between. [25]

Segments

Busnardo *et al.* studied the anatomicosurgical segments of the human pancreas in 30 corrosion casts. Two segments were found, similar to those of the liver. The right (cephalocervical) and left (corporocaudate) segments of the pancreas are separated by a poorly vascularized area.

They are connected by the pancreatic duct and often, according to these authors, by a small artery. Both segments can be used for transplantation.

Pancreatic Ducts

The main duct was first described by Wirsung in 1642. The accessory duct and minor duodenal papilla were described by Santorini in 1724, but the findings were not published until 1775. [25]

Several researchers studied the pancreas through the years, but the greatest understanding of the anatomy of the pancreatic ducts, their sphincters, and the duodenal wall has come from studies that Boyden conducted over almost 50 years (1926 to 1971). [25]

Major Duodenal Papilla and Hepatopancreatic Ampulla

There is confusion in the literature about the correct name, definition, and distinguishing points of the major duodenal papilla (often referred to as the papilla of Vater) and the hepatopancreatic or biliaropancreatic ampulla (often referred to as ampulla of Vater) [26]. The papilla is a nipplelike projection of duodenal mucosa, located where the main pancreatic duct and the CBD drain into the duodenum. The hepatopancreatic ampulla, which can have several variations, is the union of the pancreaticobiliary ducts. [26]

Major Duodenal Papilla

This papilla often bears the name of Abraham Vater (1684–1751), but the eponym is historically incorrect. The most useful term is major (or greater) duodenal papilla. [27]

The papilla is situated on the posteromedial wall of the second portion of the duodenum, 7 to 10 cm from the pylorus. Rarely, the papilla may be in the third portion of the duodenum. [27]

Hepatopancreatic (Biliaropancreatic) Ampulla

Although the ampulla is named after Vater, there is much evidence that it was first described by Santorini. Vater actually described a diverticulum of duodenal mucosa, now referred to as perivaterian diverticulum. [27]

The location, or implantation, of the junction of the main pancreatic duct and the CBD is in the descending portion of the duodenum in 75% of cases; in 25% it is primarily in the

horizontal portion of the duodenum, to the right of the superior mesenteric vessels, according to Avisse et al. [28]

Sphincter of Boyden/Sphincter of Oddi

The present concept is that several sphincters of smooth-muscle fibers surround the intramural part of the CBD, the main pancreatic duct, and the ampulla, if present. [29]The complex has a separate embryonic origin from that of the duodenal musculature and is functionally separate. Although the anatomy has been well described by Boyden and others, the terminology is unsettled. We call the entire sphincter complex the sphincter of Boyden in recognition of his contribution to the anatomy of this region, but it was originally described by Oddi in 1887, and some authors refer to it as the sphincter of Oddi. [30]

The total length of the sphincteric complex may be as short as 6 mm or as long as 30 mm, depending on the obliquity of the path taken by the biliary and pancreatic ducts through the duodenal wall.

Minor Duodenal Papilla

The minor duodenal papilla is situated approximately 2 cm cranial and slightly anterior to the major papilla. It is smaller, and its site does not have the characteristic mucosal folds that mark the site of the major papilla. [31]

Arterial Supply of the Pancreas

Van Damme wrote that the most important pancreatic artery is the splenic artery. [32] The pancreas is supplied with blood from branches arising from both the celiac trunk and the SMA. Variations are common, the head of the pancreas and the concave surface of the duodenum are supplied by two pancreaticoduodenal arterial arcades that are always present. These are formed by a pair (anterior and posterior) of superior arteries from the gastroduodenal branch of the celiac trunk that join a second pair of inferior arteries from the superior mesenteric artery. These vascular arcades lie on the surface of the pancreas but also supply the duodenal wall. [33]

Pancreatic Arcades

The gastroduodenal artery arises as one of the two terminal branches of the common hepatic artery of the celiac trunk. Shortly after it arises from the common hepatic artery branch, the gastroduodenal artery gives origin to the supraduodenal, retroduodenal, and posterior superior pancreaticoduodenal (PSPD) arteries. The supraduodenal and retroduodenal arteries arise, variably, as branches of the PSPD artery. The gastroduodenal artery ends by dividing into the right gastroepiploic and ASPD arteries. [34]

Venous Drainage of the Pancreas

In general, the veins of the pancreas parallel the arteries and lie superficial to them. Both lie posterior to the ducts in the body and tail of the pancreas. The drainage is to the portal vein, the splenic vein, and the superior and inferior mesenteric veins. [35]

Lymphatic Drainage of the Pancreas

As might be expected from the position of the pancreas, lymphatic drainage is centrifugal to the surrounding nodes .None of the efforts to demarcate specific drainage areas of the pancreas have gained wide acceptance, thus no "standard terminology" for the nodes exists. [35]

Nerve Supply of the Pancreas

Innervation of the pancreas is by the sympathetic division of the autonomic nervous system through the splanchnic nerves and by the parasympathetic division through the vagus nerve. These nerves generally follow blood vessels to their destinations. The sympathetic and parasympathetic divisions provide efferent (motor) fibers to the wall of the blood vessels, the pancreatic duct, and pancreatic acini. Further, both contain visceral afferent (pain) fibers. The distribution of these in the pancreas, however, is not well understood. [35]

Pathology

Acute pancreatitis is an acute inflammatory process of the pancreas that can involve peripancreatic tissues or remote organ systems, or both. [36] It may occur as an isolated attack or recur in distinct episodes with reversion to normal histology between attacks. By definition, acute pancreatitis is reversible; it is distinguished from chronic pancreatitis by the absence of continuing inflammation, irreversible structural changes, and permanent impairment of exocrine and endocrine pancreatic function. As the diagnosis of acute pancreatitis is usually made on clinical grounds and pancreatic tissue is rarely available, it can be difficult to distinguish between acute and chronic pancreatitis in the individual case.

The most commonly used classification system for acute pancreatitis distinguishes between mild and severe disease. [37] Severe disease is characterized by organ failure or local complications such as necrosis, pseudocysts, or fistulae. Scoring systems use prognostic signs to stratify patients and help in the early recognition of patients with a high probability of developing severe pancreatitis.

The early stages of acute pancreatitis are characterized by interstitial oedema within the pancreatic parenchyma and necrosis of peripancreatic fat. The disease may progress to coagulation necrosis of glandular elements and the surrounding fatty tissue, a condition described as necrotizing pancreatitis. Premature activation of pancreatic enzymes is the central event in the pathogenesis of acute pancreatitis. [38] Once activated, trypsin can activate many other enzymes, including kallikrein, phospholipase A2, and elastase. [39] This leads to autodigestion of pancreatic tissue as well as systemic effects from circulating enzymes causing vasodilation, increased capillary permeability with leaking of fluid into the third space, and disseminated intravascular coagulation. In the most severe cases, the result is circulatory collapse, renal insufficiency, and respiratory failure. Despite extensive research, the mechanism(s) that trigger the initial sequence of enzymatic activations remain incompletely understood. Factors that can initiate this process include acute obstruction of the pancreatic duct, exposure to toxins and venoms, and ischaemia. [40] Once initiated, the biochemical and pathophysiological processes resulting in acute pancreatitis cannot be inhibited or reversed. Treatments aimed at halting

the cycle of pancreatic autodigestion (glucagon, somatostatin, anticholinergics) have generally been disappointing. A recent meta-analysis of six trials using somatostatin showed a small benefit, but further research is needed before this drug should be routinely considered. [41] Efforts to prevent acute pancreatitis in well defined subgroups of patients (such as those undergoing endoscope retrograde cholangiopancreatography (ERCP)) have yielded more encouraging results. A recent European trial using intravenous infusion of gabexate to prevent post-ERCP pancreatitis found this drug to be efficacious, although cumbersome to administer. [42]

Progression of pathophysiology

Acute pancreatitis can be further divided in mild and severe pancreatitis. Mostly the Atlanta classification (1992) is used. In severe pancreatitis serious amount of necrosis determine the further clinical outcome. [43] About 20% of the acute pancreatitis is severe with a mortality of about 20%. This is an important classification as severe pancreatitis will need intensive care therapy whereas mild pancreatitis can be treated on the common ward. [44]

Necrosis will be followed by a systemic inflammation response syndrome (SIRS) and will determine the immediate clinical course. The further clinical course is then determined by bacterial infection. SIRS is the cause of bacterial (Gram negative) translocation from the patient's colon. [45]

Prognostic indices

In predicting the prognosis, there are several scoring indices that have been used as predictors of survival. Two such scoring systems are the Ranson's and APACHE II indices. Most but not all studies report that the APACHE score may be more accurate. In the negative study of the APACHE II, the 24 hr score was used rather than the 48 hour score. [46, 47, 48, 49] In addition, all patients in the study received at ultrasound twice which may have influenced allocation of co-interventions. Regardless, only the APACHE II can be fully calculated upon admission. As the APACHE II is more cumbersome to calculate,

presumably patients whose only laboratory abnormality is an elevated lipase or amylase do not need prognostication with the APACHE II; however, this approach is not studied.

Practice guidelines state: 2006: "The two tests that are most helpful at admission in distinguishing mild from severe acute pancreatitis are APACHE-II score and serum hematocrit. It is recommended that APACHE-II scores be generated during the first 3 days of hospitalization and thereafter as needed to help in this distinction. It is also recommended that serum hematocrit be obtained at admission, 12 h after admission, and 24 h after admission to help gauge adequacy of fluid resuscitation." [50] 2005: "Immediate assessment should include clinical evaluation, particularly of any cardiovascular, respiratory, and renal compromise, body mass index, chest x ray, and APACHE II score". [51]

Ranson's criteria

It was introduced in 1974. [52]

Parameters used:

At admission:

1. age in years >55years
2. white blood cell count > 16000/mcL
3. blood glucose > 11 mmol/L (>200 mg/dL)
4. serum AST > 250 IU/L
5. serum LDH > 350 IU/L

After 48 hours:

1. Hematocrit fall > 10%
2. increase in BUN by 1.8 or more mmol/L (5 or more mg/dL) after IV fluid hydration
3. hypocalcaemia (serum calcium < 2.0 mmol/L (<8.0 mg/dL))
4. hypoxemia (PO_2 < 60 mmHg)
5. Base deficit > 4Meq/L
6. Estimated fluid sequestration > 6L

The criteria for point assignment are that a certain breakpoint be met at anytime during that 48 hour period, so that in some situations it can be calculated shortly after admission. It is applicable to both biliary and alcoholic pancreatitis. [53]

Interpretation

If the score is greater or equal to three, severe pancreatitis likely.

If the score is less than three, severe pancreatitis is unlikely. [53]

Or

Score 0 to 2: 2% mortality

Score 3 to 4: 15% mortality

Score 5 to 6: 40% mortality

Score 7 to 8: 100% mortality

APACHE

It was introduced in 1985

"Acute Physiology and Chronic Health Evaluation score > 8 points predicts 11% to 18% mortality. [54]

- Hemorrhagic peritoneal fluid
- Obesity
- Indicators of organ failure
- Hypotension (SBP <90 mmHG) or tachycardia > 130 beats/min
- PO_2 <60 mmHg
- Oliguria (<50 mL/h) or increasing BUN and creatinine
- Serum calcium < 1.90 mmol/L (<8.0 mg/dL)
- serum albumin <33 g/L (<3.2.g/dL)

Race

The annual incidence of acute pancreatitis in Native Americans is 4 per 100,000 population; in whites, 5.7 per 100,000 population; and in blacks, 20.7 per 100,000 population. [55]

Sex

No predilection exists.

Age

The risk for African Americans aged 35-64 years is 10 times higher than for any other group. African Americans are at higher risk than whites in that same age group. [56]

Clinical Presentation

The hallmark of acute pancreatitis is a continuous, boring epigastric pain. It is usually poorly localized, is often worse in the supine position, and radiates to the back in about 50% of patients. In contrast to the often abrupt onset of pain that accompanies perforation of an abdominal viscus, the pain increases in severity to a peak in 30 to 60 minutes, then remains steady for many hours or days. Localized epigastric tenderness can be intense, but signs of peritoneal irritation such as rebound tenderness are typically absent on initial presentation, consistent with the retroperitoneal location of the pancreas. Acute ischaemia of the bowel should be considered in the differential diagnosis. [57]

Most patients have nausea and vomiting; if severe, this is an indication for continuous or periodic aspiration of stomach contents. A nasogastric tube is not necessary in mild pancreatitis. Vomiting and massive third space losses can rapidly lead to depletion of intravascular volume. The patient's urine output should be documented accurately (which may require placing a urinary catheter) and signs of dehydration treated promptly with intravenous fluids. A low grade fever (37.7-38.3°C) without other evidence of an ongoing infectious process, pancreatitis is not an indication for empirical treatment with antibiotics, but the patient must be watched for signs of systemic infection. [58]

Abdominal distension is common in acute pancreatitis. Leakage of fluid into the retroperitoneum the body's effort to dilute pancreatic enzymes and thereby contain the ravages of autodigestion causes the abdominal contents to be pushed forward. This protrusion of abdominal contents, exacerbated by loops of bowel filled by gas and fluid from the almost inevitable small bowel ileus, may grossly distend the abdomen. The almost universal ileus of all but mild pancreatitis may be exacerbated by the narcotic analgesia needed to treat the intense pain of this condition. Evidence of retroperitoneal hemorrhage, specifically periumbilical bruising (Cullen's sign) and flank bruising (Grey-Turner's sign) is rare but should be sought as a prognostic indicator.[27]

Respiratory problems are common in acute pancreatitis. The tendency to hypoventilation may be exacerbated by basal pleural effusions and atelectasis. The most severe respiratory complication of acute pancreatitis, adult respiratory distress syndrome, is rare but potentially fatal. These patients usually require ventilatory support. In a recent British study of acute pancreatitis with fatal outcome, respiratory failure was more common than infection or sepsis. [60]

Hypocalcaemia is common (due to saponification of fat) but tetany (due to loss of ionised calcium) is rare. Hypocalcaemia is a negative prognostic factor; significant hypocalcaemia (after correction for serum concentration of albumin, which is also often low) should be treated by intravenous replacement. [61]

History

The main presentation of acute pancreatitis is epigastric pain or right upper quadrant pain radiating to the back associated with nausea and vomiting and lesser proportion of patients with mild fever and jaundice.

The patient should be asked about recent surgeries and invasive procedures (endoscopic retrograde cholangiopancreatography) or family history hypertriglyceridemia.

Patients frequently have a history of previous biliary colic and binge alcohol consumption, the major causes of acute pancreatitis.

Physical findings:

Tachycardia

Tachypnea

Hypotension

Fever

Abdominal tenderness, distension, guarding, and rigidity

Mild jaundice

Diminished or absent bowel sounds

Because of contiguous spread of inflammation (effusion) from the pancreas, lung auscultation may reveal basilar rales, especially in the left lung.

Occasionally, in the extremities, muscular spasm may be noted secondary to hypocalcaemia.

Severe cases may have a Grey Turner's sign and Cullen sign caused by the retroperitoneal leak of blood from the pancreas in hemorrhagic pancreatitis. [62]

Causes

The major causes are long-standing alcohol consumption and biliary stone disease. In developed countries, the most common cause of acute pancreatitis is alcohol abuse. On the cellular level, ethanol leads to intracellular accumulation of digestive enzymes and their premature activation and release.

On the ductal level, ethanol increases the permeability of ductules, which allow enzymes to reach the parenchyma, resulting in pancreatic damage.

Ethanol increases the protein content of the pancreatic juice and decreases bicarbonate levels and trypsin inhibitor concentrations. This leads to the formation of protein plugs that block the pancreatic outflow and obstruction.

Another major cause of acute pancreatitis is biliary stone disease (e.g., cholelithiasis, choledocholithiasis). A biliary stone may lodge in the pancreatic duct or ampulla of Vater and obstruct the pancreatic duct, leading to extravasation of enzymes into the parenchyma. [63]

Minor causes of acute pancreatitis

The use of certain medications have been associated as causative agent for acute pancreatitis, including azathioprine, corticosteroids, sulfonamides, thiazides, furosemides, nonsteroidal anti-inflammatory drugs (NSAIDs), mercaptopurine, methyldopa, and tetracyclines . [64]

Endoscopic retrograde cholangiopancreatography (ERCP)

Hypertriglyceridemia (When the triglyceride level exceeds 1000 mg/U, an episode of pancreatitis is more likely.)

Peptic ulcer disease

Abdominal or cardiopulmonary bypass surgery, which may insult the gland by ischemia

Trauma to the abdomen or back, resulting in sudden compression of the gland against the spine posteriorly

Carcinoma of the pancreas, which may lead to pancreatic outflow obstruction

Viral infections, including mumps, coxsackievirus, cytomegalovirus (CMV), hepatitis virus, Epstein-Barr virus (EBV), and rubella

Bacterial infections, such as mycoplasma

Intestinal parasites, such as Ascaris, which can block the pancreatic outflow

Pancreas divisum

Scorpion and snake bites

Vascular factors, such as ischemia or vasculitis. [65]

Investigations

Blood Investigations - Full blood count, renal function tests, liver function, serum calcium, serum amylase and lipase, Arterial blood gas

Imaging - Chest Xray (for exclusion of perforated viscus), Abdominal Xrays (for detection of "sentinel loop" dilated duodenum sign, and gallstones which are radioopaque in 10%) and CT abdomen. [66]

Amylase and lipase

Serum amylase rises 2 to 12 hours from the onset of symptoms, and normalizes within 1 week. [67]Serum lipase rises 4 to 8 hours from the onset of symptoms and normalizes within 8 to 14 days. [68]Serum amylase may be normal (in 10% of cases) for cases of acute on chronic pancreatitis (depleted acini cell mass) and hypertriglyceridemia

Reasons for false positive elevated serum amylase include salivary gland disease (elevated salivary amylase) and macroamylasemia

If Lipase level is about 2.5 to 3 times that of Amylase, it is an indication of pancreatitis due to Alcohol. [69]

Regarding selection of these tests, two practice guidelines state:" It is usually not necessary to measure both serum amylase and lipase. Serum lipase may be preferable because it remains normal in some nonpancreatic conditions that increase serum amylase including macroamylasemia, parotitis, and some carcinomas. In general, serum lipase is thought to be more sensitive and specific than serum amylase in the diagnosis of acute pancreatitis" [70]

"Although amylase is widely available and provides acceptable accuracy of diagnosis, where lipase is available it is preferred for the diagnosis of acute pancreatitis (recommendation grade A)" [71]

Most, but not individual studies support the superiority of the lipase. In one large study, there were no patients with pancreatitis who had an elevated amylase with a normal lipase.[72] Another study found that the amylase could add diagnostic value to the lipase, but only if the results of the two tests were combined with a discriminant function equation.[73]

Computed tomography

Regarding the need for computed tomography, practice guidelines state:

2006: "Many patients with acute pancreatitis do not require a CT scan at admission or at any time during the hospitalization. For example, a CT scan is usually not essential in patients with recurrent mild pancreatitis caused by alcohol. A reasonable indication for a CT scan at admission (but not necessarily a CT with IV contrast) is to distinguish acute pancreatitis from another serious intra-abdominal condition, such as a perforated ulcer."[74]

2005: "Patients with persisting organ failure, signs of sepsis, or deterioration in clinical status 6–10 days after admission will require CT (recommendation grade B)." [75]

CT abdomen should not be performed before the first 48 hours of onset of symptoms as early CT (<48 h) may result in equivocal or normal findings.

CT Findings can be classified into the following categories:

- Intrapancreatic - diffuse or segmental enlargement, edema, gas bubbles, pancreatic pseudocysts and phlegmons/abscesses (which present 4 to 6 wks after initial onset)
- Peripancreatic / extrapancreatic - irregular pancreatic outline, obliterated peripancreatic fat, retroperitoneal edema, fluid in the lessar sac, fluid in the left anterior pararenal space
- Locoregional - Gerota's fascia sign (thickening of inflamed Gerota's fascia, which becomes visible), pancreatic ascites, pleural effusion (seen on basal cuts of the pleural cavity), adynamic ileus.

Balthazar Scoring for the Grading of Acute Pancreatitis

- Grade A - normal CT
- Grade B - focal or diffuse enlargement of the pancreas
- Grade C - pancreatic gland abnormalities and peripancreatic inflammation
- Grade D - fluid collection in a single location
- Grade E - two or more collections and/or gas bubbles in or adjacent to pancreas

CT severity index = CT grade point + points for necrosis Grade Points

- Grade A 0
- Grade B 1
- Grade C 2
- Grade D 3
- Grade E 4

Necrosis percentage Points

- 0 0
- <30 %..... 2
- 30-50%..... 4
- >50%..... 6

CT grade points are added to points assigned for percentage of necrosis to determine the CT severity index. [75]

Magnetic resonance imaging

One study found that a nonenhanced magnetic resonance imaging (MRI) was comparable to contrast-enhanced computed tomography (CT). [76]

Mortality/Morbidity

Although acute pancreatitis should be noted, chronic pancreatitis has a more severe presentation as episodes recur. [77] Acute respiratory distress syndrome (ARDS), acute renal failure, cardiac depression, hemorrhage, and hypotensive shock all may be systemic manifestations of acute pancreatitis in its most severe form.

Mild edematous pancreatitis occurs in about 80% of presentations, and the mortality rate is below 1%. [78]Severe acute pancreatitis occurs in about 20% of presentations, with a mortality rate reaching 24%.

Treatment

Medical treatment consists of the following:

Fluid resuscitation and hydration: Patients with acute pancreatitis lose a large amount of fluids to third spacing into the retro peritoneum and intra-abdominal area. These fluids have to be replaced promptly within the first 24 hours with both crystalline and colloid solutions, sometimes reaching 10 L. [79]

Central venous pressure, pulmonary artery wedge pressure, and urine output (>0.5 mL/kg/h) can be followed up as markers of adequate hydration.

The previously followed rule of NPO has changed, and prospective randomized controlled trials have showed that enteral tube feeding is superior to parenteral nutrition to avoid malnutrition and reverse the catabolic state of these patients. [80]

Adequate analgesia: Opiate derivatives and epidural analgesia can be added if needed. Antibiotic coverage is needed to prevent gram-negative sepsis.

Pain control

Analgesics are used to relieve pain. Meperidine is preferred over morphine because of the greater spastic effect of the latter on the sphincter of Oddi. [81]

Bowel rest

In the management of acute pancreatitis, the treatment is to stop feeding the patient, giving him or her nothing by mouth, giving intravenous fluids to prevent dehydration, and sufficient pain control. As the pancreas is stimulated to secrete enzymes by the presence of food in the stomach, having no food pass through the system allows the pancreas to rest. Approximately 20% of patients have a relapse of pain during acute pancreatitis. [82] Approximately 75% of relapses occur within 48 hours of oral refeeding.

The incidence of relapse after oral refeeding may be reduced by post-pyloric enteral rather than parenteral feeding prior to oral refeeding. [83]

Nutritional support

Recently, there has been a shift in the management paradigm from TPN (total parenteral nutrition) to early, post-pyloric enteral feeding (in which a feeding tube is endoscopically or radiographically introduced to the third portion of the duodenum). The advantage of enteral feeding is that it is more physiological, prevents gut mucosal atrophy, and is free from the side effects of TPN (such as fungemia). The additional advantages of post-pyloric feeding are the inverse relationship of pancreatic exocrine secretions and distance of nutrient delivery from the pylorus, as well as reduced risk of aspiration.

Disadvantages of a naso-enteric feeding tube include increased risk of sinusitis (especially if the tube remains in place greater than two weeks) and a still-present risk of accidentally intubating the bronchus even in intubated patients (contrary to popular belief, the endotracheal tube cuff alone is not always sufficient to prevent NG tube entry into the trachea). [84]

Antibiotics

A meta-analysis by the Cochrane Collaboration concluded that antibiotics help to reduce mortality. [85] However, the one study in the meta-analysis that used a quinolone, and a subsequent randomized controlled trial that studied ciprofloxacin were both negative. [86]

An early randomized controlled trial of imipenem 0.5 gram intravenously every eight hours for two weeks showed a reduction in from pancreatic sepsis from 30% to 12%. [87]

Another randomized controlled trial with patients who had at least 50% pancreatic necrosis found a benefit from imipenem compared to pefloxacin with a reduction in infected necrosis from 34% to 20%.[88]

A subsequent randomized controlled trial that used meropenem 1 gram intravenously every 8 hours for 7 to 21 days stated no benefit; however, 28% of patients in the group subsequently required open antibiotic treatment vs. 46% in the placebo group. In addition, the control group had only 18% incidence of peripancreatic infections and less biliary pancreatitis that the treatment group (44% versus 24%). [89]

In summary, the role of antibiotics is controversial. [90,91] One recent expert opinion (prior to the last negative trial of meropenem) suggested the use of imipenem if CT scan showed more than 30% necrosis of the pancreas is beneficial.

ERCP

Early ERCP (endoscopic retrograde cholangiopancreatography), performed within 24 hours of presentation, is known to reduce morbidity and mortality [92] The indications for early ERCP are as follows:

- Clinical deterioration or lack of improvement after 24 hours
- Detection of common bile duct stones or dilated intrahepatic or extrahepatic ducts on CT abdomen

The disadvantages of ERCP are as follows:

- ERCP precipitates pancreatitis, and can introduce infection to sterile pancreatitis
- The inherent risks of ERCP i.e. bleeding

It is worth noting that ERCP itself can be a cause of pancreatitis.

Surgery

Surgery is indicated for (I) infected pancreatic necrosis and (ii) diagnostic uncertainty and (iii) complications. The most common cause of death in acute pancreatitis is secondary infection. Infection is diagnosed based on 2 criteria

- Gas bubbles on CT scan (present in 20 to 50% of infected necrosis)
- Positive bacterial culture on FNA (fine needle aspiration, usually CT or US guided) of the pancreas.

Surgical options for infected necrosis include:[93]

- Conventional management - necrosectomy with simple drainage
- Closed management - necrosectomy with closed continuous lavage
- Open management - necrosectomy with planned staged reoperations at definite intervals (up to 7 reoperations in some cases)

Other measures

- Enzyme inhibitors are not proven to work.
- The use of octreotide has not been shown to improve outcome

Complications

Complications can be systemic or locoregional.

Systemic complications include ARDS, multiple organ dysfunction syndrome, DIC, hypocalcemia (from fat saponification), hyperglycemia and insulin dependent diabetes mellitus (from pancreatic insulin producing beta cell damage)

Locoregional complications include pancreatic pseudocyst and phlegmon / abscess formation, splenic artery pseudoaneurysms, hemorrhage from erosions into splenic artery and vein, thrombosis of the splenic vein, superior mesenteric vein and portal veins (in

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Locoregional complications include pancreatic pseudocyst and phlegmon / abscess formation, splenic artery pseudoaneurysms, hemorrhage from erosions into splenic artery and vein, thrombosis of the splenic vein, superior mesenteric vein and portal veins (in

descending order of frequency), duodenal obstruction, common bile duct obstruction, progression to chronic pancreatitis .[94]

Neri V *et al* Division of General Surgery, Department of Surgical Sciences, University of Foggia, Polyclinic of Foggia. Foggia, Italy, had conducted a study comparing hemoconcentration and ranson's criteria on patients admitted with acute pancreatitis from January 1998 to June 2005 to there centre. Had showed an association between pancreatic necrosis, by means of CT evaluation, and the hemoconcentration. Hematocrit more than 43% in the males and more than 39% in the females and/or a reduction of the Hct within the first 24 hours from the admission, were markers of severity and pancreatic necrosis (and organ failure). In 6 of the 7 patients with necrotizing pancreatitis there was critical value of Hct and only in 4 of the 17 patients with edematous pancreatitis there was a high value of Hct, showing the statistical significativity of the proposed criteria ($P<0.01$). The negative predictive value of the hemoconcentration was 94.7% for the evolution in pancreatic necrosis. [95]

Paul Georg Lankisch *et al*, from the Department of Internal Medicine, Municipal Clinic of Lüneburg, Germany had conducted a study between 1988 to 1999 for 316 patients (202 male, 114 female) with a first attack of acute pancreatitis. The role of the hematocrit as an early marker of severe and/or necrotizing pancreatitis has been retrospectively evaluated against the prospectively obtained data. Hematocrit, as a single parameter measured on admission, had the same sensitivity and negative predictive value as the more complicated Ranson's and Imrie scores obtained only after 48 h. However, its specificity, positive predictive value, and total accuracy were lower. Hemoconcentration significantly correlated with the Balthazar score (differential diagnosis between interstitial and necrotizing pancreatitis), stay in ICU, and total hospital stay. Sensitivity and specificity of the hematocrit cut-off level of 43.0% for male and 39.6% for female patients to detect necrotizing pancreatitis were 74% and 45%, respectively. The positive predictive value was 24% and the negative predictive value 88%. Receiver operation characteristics (ROC) curve values for several cut-offs did not result in more ideal levels.[96]

Baillargeon JD,*et al* from Center for Pancreatic Disease, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115, USA. From May 1992 to June 1996, had conducted a case-control study with necrotizing pancreatitis. And had compared with another group of patients with acute pancreatitis. There were 32 patients in each group. Logistic regression identified an admission hematocrit of ≥ 47% and a failure of admission hematocrit to decrease at 24 h as the best binary risk factors for necrotizing pancreatitis. At admission, more patients with necrotizing pancreatitis than with mild pancreatitis had a hematocrit ≥ 47% (11/32 vs. 3/32; $p = 0.03$). At 24 h, 15 additional patients with necrotizing pancreatitis versus only one with mild pancreatitis showed no decrease in admission hematocrit ($p < 0.01$). Thus, by 24 h, 26 of 32 patients with necrotizing pancreatitis versus only four of 32 patients with mild pancreatitis met one or the other criterion ($p < 0.01$). The sensitivity and specificity at admission were 34% and 91%; at 24 h, 81% and 88%.[97]

AIM OF THE STUDY

To determine the role of hemoconcentration in progression of acute pancreatitis.

OBJECTIVES OF THE STUDY:

- To find the demographic profile of patients with acute pancreatitis
- To compare the prognostic accuracy of hemoconcentration in diagnosis of acute pancreatitis with that of Ranson's criteria
- To evaluate the role of hemoconcentration to predict severity of acute pancreatitis

PATIENTS AND METHODS

A prospective study was carried out from July 2006 to June 2007 at Department of Surgery, Tribhuvan University Teaching Hospital (TUTH), and Kathmandu, Nepal for a period of one year. A total of seventy seven consecutive patients with the clinical diagnosis of acute pancreatitis that had undergone admission and treatment were included in the study.

Inclusion criteria:

All patients admitted with the clinical diagnosis of acute pancreatitis who subsequently underwent admission and treatment were included.

Exclusion criteria:

The following patients were excluded from the study:

1. Patients with severe pancreatitis
2. Patients not giving consent
3. Patients with recurrent attacks of pancreatitis

METHODOLOGY

The initial evaluation and assessment of patients was done by a surgery resident on call/ faculty at Emergency Department of TUTH. A detailed history was sought; examination findings and routine investigations reports were recorded on a prepared Proforma. The initial diagnosis of acute pancreatitis was based on the clinical evaluation supported by raised serum amylase level at least four times the normal. Patients considered to have acute pancreatitis on evaluation were admitted for further evaluation and treatment. In the patients with the clinical diagnosis of acute pancreatitis, Ranson's scoring was done and also hematocrit.

Approval from the institute research committee was taken. Informed consent was obtained from all patients admitted with diagnosis of acute pancreatitis. In all patients giving consent and qualifying the above criteria, necessary investigations were sent to calculate Ranson's score at admission and at forty eight hours. All patients with the diagnosis of acute pancreatitis underwent admission and treatment in the respective general surgical units under the supervision of the consultant surgeon respectively. The report of hematocrit was however not made available to the evaluating surgeon for decision making.

Ranson's scoring, as discussed previously, along with hematocrit at admission was applied to all patients with history suggestive of acute pancreatitis based on the clinical and laboratory results at emergency.

Hemoconcentration was defined as a hematocrit level greater than 43.0% for male and a hematocrit greater than 39.6% for female patients.

The findings were noted Ranson's criteria used to calculate a score for each patient at admission and at forty eight hours the hemoconcentration tabulated respectively. Patients with a total Ranson's score less than three at 48 hours were labeled as having mild disease and that of greater than three were deemed to have severe disease. Computer tomographic (C-T) scans were done in patients with a doubtful diagnosis at

admission or patient who had clinical features of having a complication(s) after seventy two hours of admission who did not respond to treatment.

The reports were subsequently followed up and recorded in the preformed Proforma.

OBSERVATION AND RESULTS

STATISTICAL ANALYSIS

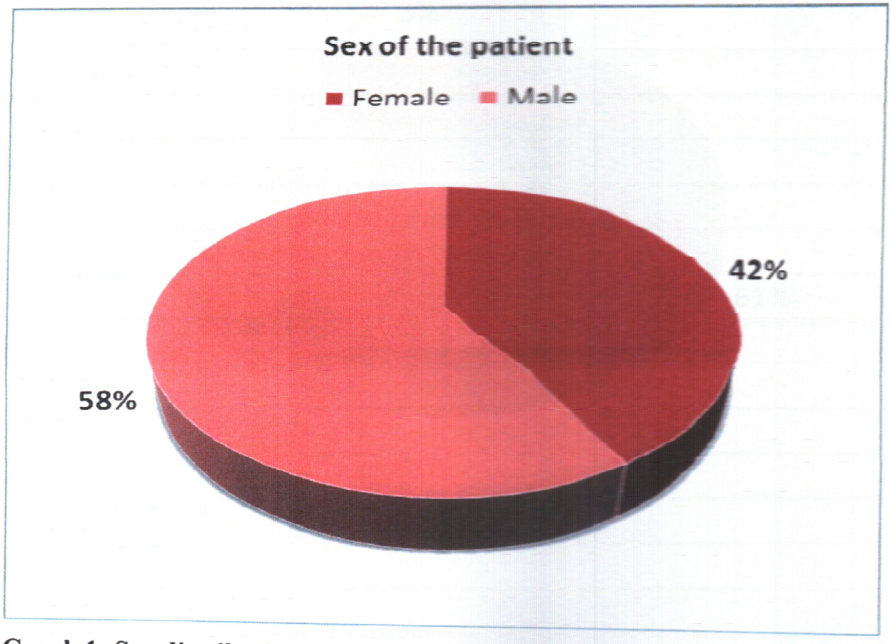
Statistical tools and parameters used were:

1. SPSS software version 10.0 was used.
2. Frequencies/ percentages, validity of hemoconcentration to predict severe acute pancreatitis were calculated.
3. Findings are presented as tables, bar diagrams, pie-charts and scatterogram.
4. Statistical tests applied:
    a. Chi-square test: used to compare the frequency/proportion between the two groups
    b. Spearman's rho test: used to compare the significance of correlation between hemoconcentration and Ranson's score.

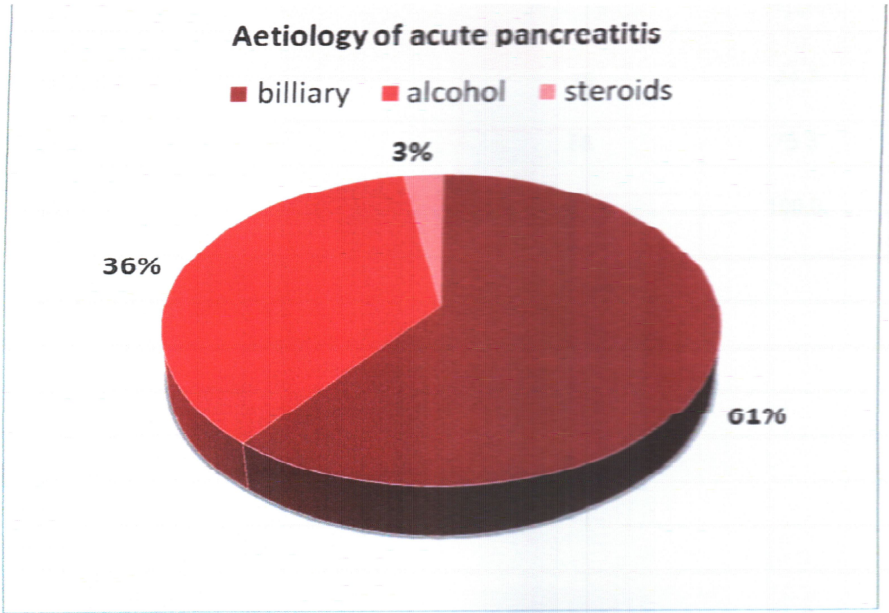
Table 1: Age of the patient

	Frequency	Percent
16-30 years	12	15.6
31-45 years	28	36.4
46-60 years	19	24.7
> 60 years	18	23.4
Total	77	100.0

	Years
Mean	46.97
Median	45.00
Std. Deviation	15.58
Range	68
Minimum	16
Maximum	04



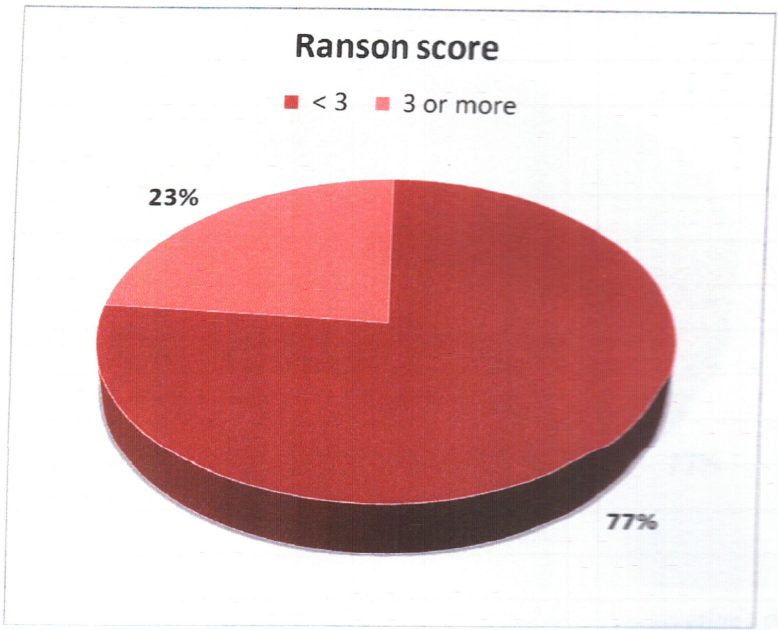
Graph 1: Sex distribution



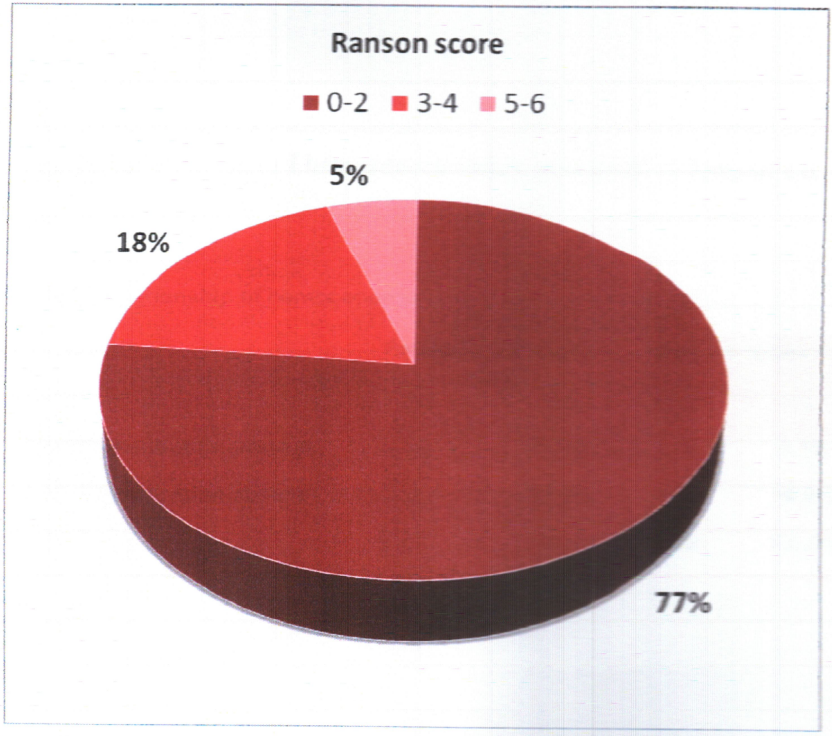
Graph 2: Aetiology of acute pancreatitis

Table 2: Hemoconcentration*

	Frequency	Percent
present	19	24.7
absent	58	75.3
Total	77	100.0



Graph 3 : Presence of hemoconcentration versus ranson's score



Graph 4: Ranson's score (compared with hemoconcentration) denoting respective mortality groups

Calculation of validity of hemoconcentration compared to Ranson's score

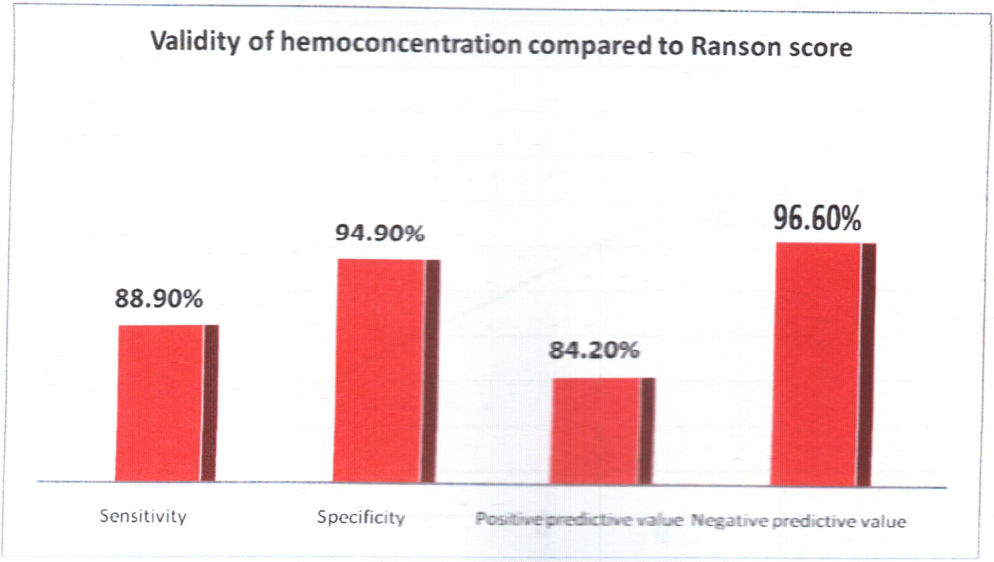
Table 3: Relationship of hemoconcentration and Ranson's score

	Ranson's score 3 or more		Rawson score < 3		p-value
	N	%	N	%	
hemoconcentration present	16	88.9%	3	5.1%	<0.001*
hemoconcentration absent	2	11.1%	56	94.9%	
Total	18	100.0%	59	100.0%	

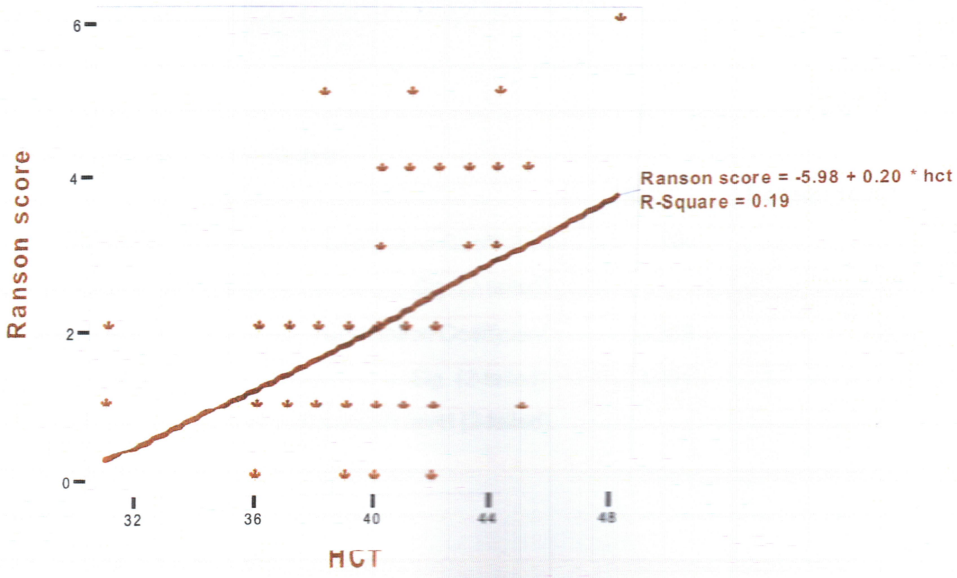
*chi-square test

Table4: verification of results of hemoconcentration and Ranson's score

	Ranson's score 3 or more		Rawson score < 3		Total	
	N	%	N	%	N	%
hemoconcentration present	16	84.2%	3	15.8%	19	100.0%
hemoconcentration absent	2	3.4%	56	96.6%	58	100.0%



Graph 5: Validity of hemoconcentration



Graph 6: scatterogram showing the correlation between hemoconcentration and Ranson's score

Table 5: Correlations tabulated

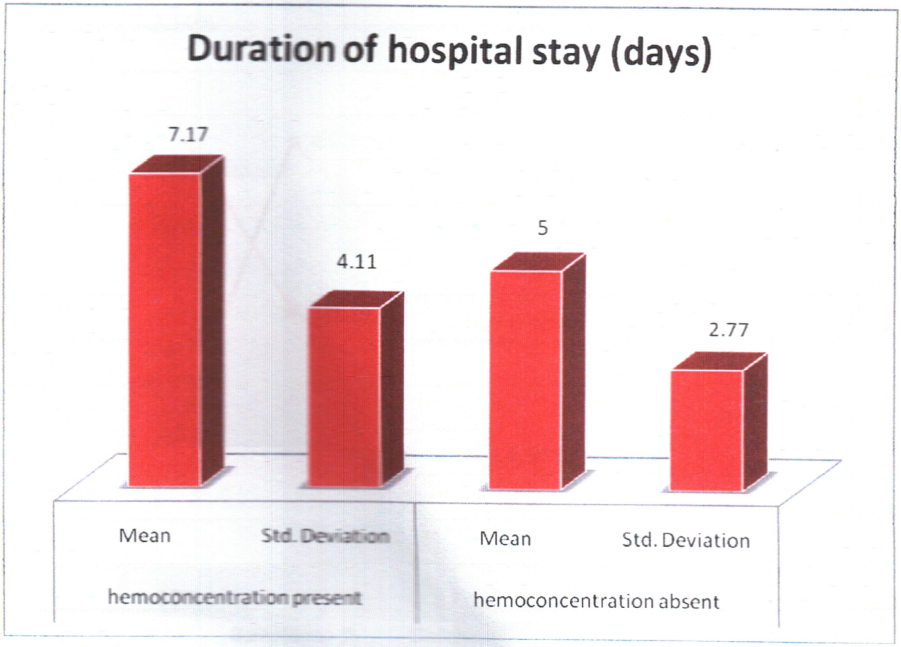
		HCT	Ranson score
HCT	Correlation Coefficient	1.000	0.368
	Sig. (2-tailed)	.	0.001
Ranson score	Correlation Coefficient	0.368	1.000
	Sig. (2-tailed)	0.001	.

- Correlation is significant at the 0.01 level (2-tailed).
- Spearman's rho test applied

Equation:

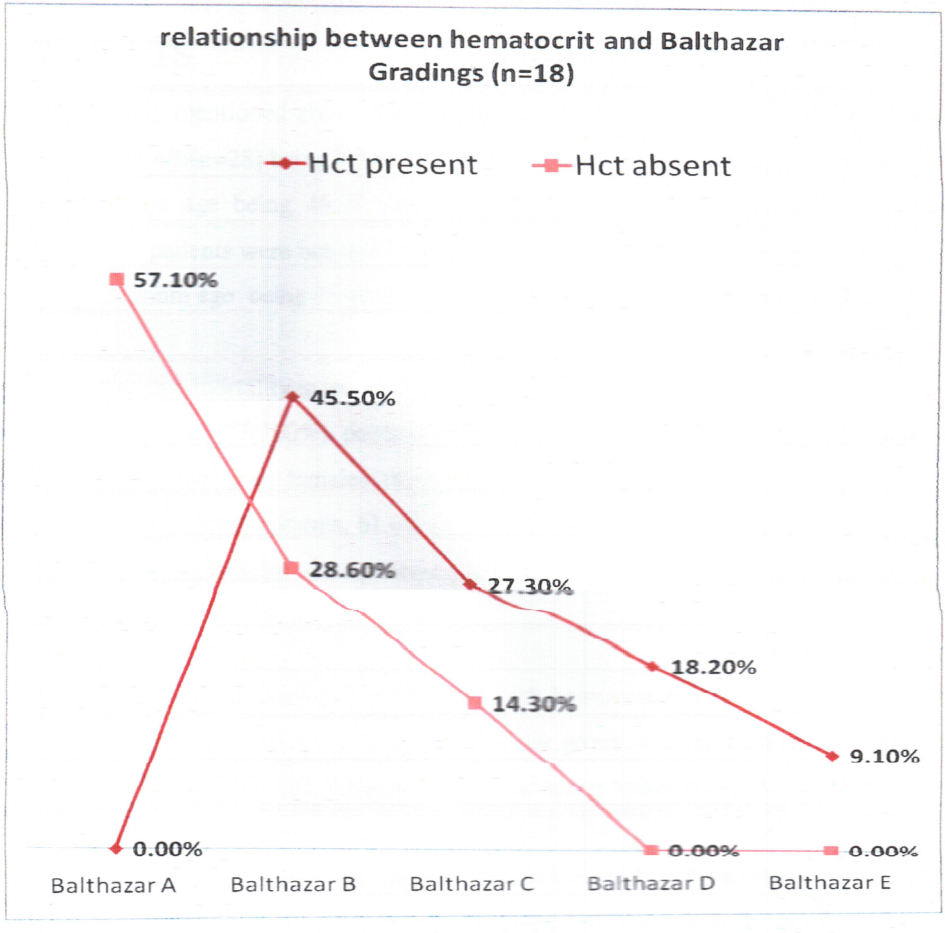
Ranson's score = -5.98 + (0.20 X Hct)

The correlation hemoconcentration versus ranson's score was shown significant at the 0.01 level.



*a single deceased case not included in the analysis (n=76)

Graph 7: Duration of Hospital stay (days)



Graph 8 Relationship between hematocrit and Balthazar Grading

RESULTS

In our study mentioned above the total number of patients were 77 (100%). Maximum patients 36.4%(n=28) being between the age of 31-45 year age group. (Table 1)

The average age being 46.97 years. The above analysis also shows that half of the number of patients were below 45.0years. The standard deviation being 15.58.

The minimum age being 16 years and the maximum age being 84 years. (Table 1)

There was one mortality in the study.

Out of the total 77(100%) patients admitted to the study, 58.4% (n=45) were males 41.6% (n=41.6%) were females. (Graph1)

Out of the 77(100%) patients, 61.0% (n = 47) had a billiary cause, with 36.4% amounting to alcohol as a cause for acute pancreatitis and 2.6% (n=2) accounting for steroid induced pancreatitis. (Graph 2)

The duration of hospital stay for patients with hemoconcentration was 7.17 days with a standard deviation of 4.11 days and that of the group without hemoconcentration had 5 days and the standard deviation was 2.77 and the p value being 0.012 between the two groups. (Graph 7)

Out of the total 77(100%) patients admitted to the study, 18 patients had undergone CT scan of abdomen no patients were present in the Balthazar A in the group with pressance of hemoconcentration, 5 patients (45.5%)in Balthazar B, 3 patients (27.3%), 2 patients(18.2%) in Balthazar D and 1 patient(9.1%) in Balthazar E.

Where as in the group who had hemoconcentration absent 4(57.1%) patients in Balthazar a,2(28.6%) patients in BalthazarB,1patient(14.3%) in Balthazar C and no patients in Balthazar D and E.(Graph 8)

The hematocrit defined as a level >43.0% for male and >39.6% for female patients. Taking total male patients and female patients combined 24.7 %(n=19) of patients exceeded the cut off values where as 75.3 %(n=58) patients did not.

Out of the total seventy seven (100%) patients 23.4% (n=18) had a Ranson's Score greater than 3 and 76.6% (n=59) had a score less than 3. (Table 2)

Out of the total seventy seven (100%) patients, 76.6% (n=59) had a score between 0-2,and 18.2%(n=14) had a score between 3-4 and 5.2%(n=4) had a score between 5-6 and hence denoting mortality in respective groups.(Graph 3)

The p value is 0.001 statistically significant

From the above statistical analysis hemoconcentration (compared to Ranson's score had a sensitivity of 88.9% and evaluated analysis also shows a specificity of 94.90% respectively. The positive predictive value is 84.2% with a negative predictive value of 96.6% respectively. (Table 3),(Table 4) and (Graph 6)

DISCUSSION

From mild disease to multiorgan failure and sepsis, acute pancreatitis is a disorder that has numerous causes, an obscure pathogenesis, few effective remedies, and an often unpredictable outcome. In 1925, Moynihan aptly described the dramatic nature of acute pancreatitis as the "most terrible of all calamities that occur in connection with the abdominal viscera. The suddenness of its onset, the illimitable agony which accompanies it and the mortality attendant upon it render it the most formidable of catastrophes". [98] Just over 100 years ago, Reginald Fitz described many of the modern clinical and pathologic features of severe acute pancreatitis. [99,100] at the turn of the century, Opie brought to light the association between cholelithiasis and acute pancreatitis. [101] it was not until 1917 that alcohol was firmly established as an important pathogenesis factor. [102]

Nearly 25 percent of all attacks of pancreatitis are severe, leading to complications and the mortality rate approaches 9 percent. [103,104,105] Some centers have noted an increase in the mortality rate over time, despite improvements in diagnosis and management, whereas others have noted a marked decrease. [106,107] the mortality rate in children has been as high as 20 to 25 percent in some series. [108,109,110] Most clinical series involving adults cite pancreatic infection as the number-one cause of death, accounting for 70 to 80 percent of deaths. A large autopsy study of 405 patients found, however, that 60 percent of deaths from acute pancreatitis occurred within the first week after admission, and pulmonary failure was more common than infection. Forty percent of patients died after the first week, with sepsis being the most common cause. [111]

Patients likely to have a severe attack are best managed in an intensive care unit. Numerous standardized tools for assessment have been developed to identify patients at risk. Ranson's criteria remain the most commonly used. [112] The five initial criteria assess the severity of the acute inflammatory process, whereas the six criteria measured at 48 hours determine the systemic effects of circulating enzymes and toxins. The presence of three or more Ranson's signs usually indicates severe pancreatitis. Mortality increases with the number of Ranson's signs (patients with ≤2 criteria, 3-4 criteria, or ≥5 criteria have death rates of <1%, 16%, and >40%, respectively). A limitation of the Ranson's

system (and of other commonly used scoring systems, such as the Glasgow criteria) is the need to wait 48 hours to obtain a complete assessment. The APACHE II system allows a more rapid determination of prognosis but is more cumbersome to use. [113,114]

Therefore early assessment of the prognosis still remains a clinical challenge at an early stage of the disease. The imaging procedures and the elevated mediators are not widely available at the beginning.

Ranson's score is an objective assessment of patient with upper abdominal pain. [115] when the score is three or more then the probability of patient with upper abdominal pain having acute pancreatitis, is said to have severe form of the disease. Along with clinical evaluation, Ranson's scoring system is widely used as a prognostic tool in our Institute.

Because of its acceptance and use in our Institute, it has been taken as the reference with which the current study is compared.

The total numbers of patients were seventy seven. The maximum patients were between 31-45 year age group. The average age being 46.97. The above analysis also shows that half the number of patients was below 45.0 years. This finding is similar to other studies mentioned in literature. [56] The standard deviation being 15.58.The Range, minimum being 16 and the maximum age being 84 years.

Out of the total patients admitted to the study, there were no sex predilection. As seen by other studies there is no significant preponderance to either sex in acute pancreatitis.[56]

Out of the seventy seven patients, forty seven patients had a billiary cause, with twenty eight patients amounting to alcohol as a cause for Acute pancreatitis and two accounting for steroid induced pancreatitis. By multivariate analysis, the factors causing acute pancreatitis had similar results accounting for major portion being gall stones and ethanol use. However due to the less number of patients and the time period in consideration, other causes of pancreatitis might have not been seen.

The hematocrit was defined as a level greater than43.0% for male and greater than 39.6% for female patients. Taking total male patients and female patients combined nineteen

patients exceeded the cut off values where as fifty eight patients did not. Out of the total seventy seven patients eighteen patients had a Ranson's Score greater than three and fifty nine patients had a score less than three. This result was coherent with other studies by Neri V *et al,* and Paul Georg Lankisch *et al.*

Out of the total seventy seven (100%) patients, 76.6% (n=59) had a score between 0-2, and 18.2% (n=14) had a score between 3-4 and 5.2% (n=4) had a score between 5-6 and hence denoting mortality in respective groups.

The difference of hospital stay for the patients having cutoff values of hemoconcentration and those who did not have hemoconcentration were statistically significant. By multivariate analysis, it has also been seen that the duration of hospital stay between mild form and severe form of pancreatitis is statistically significant.

From our study, it did not show any statistically significant correlation between hemoconcentration and Balthazar grading (CT). This is conflicting to the study conducted by Neri V *et al* where the CT findings were comparable and statistically significant to hemoconcentration. This conflicting result may be the smaller sample size used in our study that is 18 patients who had undergone CT scan examination out of the total 77 patients.

Several investigators have reported significant correlations of hemoconcentration and ranson's score. The p value was 0.001, thus statistically significant in our study. The above study also showed a positive correlation between hemoconcentration and the score of Ranson's.

From the above statistical analysis hemoconcentration (compared to Ranson's score had a sensitivity of 88.9% and evaluated analysis also shows a specificity of 94.90% respectively. The positive predictive value is 84.2% with a negative predictive value of 96.6% respectively.

Sensitivity, specificity, positive predictive value, and negative predictive value of Ranson's score to predict a severe attack were (78%-85.0%) and (80%-98%), and (70%-

80%) and (60%-70%) respectively.[116] Compared to other studies we had a comparable sensitivity (88.90%) and a specificity (94.90%). The positive predictive value being (84.20%) and negative predictive value being (96.62%) for hemoconcentration in predicting the prognosis of acute pancreatitis. This result is also similar statistically to the results achieved by Neri V *et al*, and Baillargeon JD, *et al*.[117,,121,122]

Hence hemoconcentration is a simple tool which can be used to predict the prognosis of acute pancreatitis earlier in its course as it significantly changes the aggressiveness of treatment of severe pancreatitis.[118,119,120]

80%) and (60%-70%) respectively.[116] Compared to other studies we had a comparable sensitivity (88.90%) and a specificity (94.90%). The positive predictive value being (84.20%) and negative predictive value being (96.62%) for hemoconcentration in predicting the prognosis of acute pancreatitis. This result is also similar statistically to the results achieved by Neri V *et al,* and Baillargeon JD, *et al* .[117,,121,122]

Hence hemoconcentration is a simple tool which can be used to predict the prognosis of acute pancreatitis earlier in its course as it significantly changes the aggressiveness of treatment of severe pancreatitis.[118,119,120]

CONCLUSION:

The prognostic value of hemoconcentration was comparable to Ranson's score. The major value of this single easily obtainable and cheap parameter on admission lies in its high negative predictive value.

Hemoconcentration did not predict the outcome of any one or individual complication(s) in this study.

However larger controlled clinical trials need to be conducted for verification of the role of hemoconcentration in progression of acute pancreatitis.

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APPENDIX

PROFORMA

Name: **age/sex:** **Hospital no:**

Address: occupation: DoA: DoD:

C/O:

Pain abdomen
Nausea / vomiting
Fever
Others

Predisposing factors :

Cholelithiasis	
Alcohol	
Surgery	
Trauma	
Medication	
Infection	
others	

Ranson's Criteria:

At admission:

Age: (>55 yrs)	
WBC: (16,000/ microL)	
Blood Glucose: (>10 mmol/l)	
LDH:(>350 iu/l)	
AST:(250 iu/l)	

Initial 48 hours:

Hematocrit decrease:(>10 %)	
BUN elevation:(>5 mg/dl)	
Sr Calcium:(<8 mg/dl)	
Arterial pO2:(<60 mmHg)	
Base deficit: (>4 meq/l)	
Estimated fluid sequestration: (>6L)	

Hemoglobin at admission	
Packed cell volume	
Hemoglobin at initial 48 hours	
Packed cell volume	

Other investigations:

USG ABDOMEN:

CT SCAN ABDOMEN:

Management:

Complications:

Operative intervention:

Final out come:

Remarks: