"ESTIMATION OF SERUM ESTRADIOL LEVELS AND ITS CO-RELATION WITH BISAP (BEDSIDE INDEX FOR SEVERITY IN ACUTE PANCREATITIS) SCORE IN SEVERE ACUTE PANCREATITIS – ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"

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ENDORSEMENT

This is to certify that the dissertation entitled **"ESTIMATION OF SERUM ESTRADIOL LEVELS AND ITS CO-RELATION WITH BISAP (BEDSIDE INDEX FOR SEVERITY IN ACUTE PANCREATITIS) SCORE IN SEVERE ACUTE PANCREATITIS – ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"** is a bonafide research work done by **REG NO. 2012092716.**

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LIST OF ABBREVIATIONS USED

- **ICU:**INTENSIVE CARE UNIT
- **SIRS:**SYSTEMIC INFLAMMATORY RESPONSE SYNDROME
- **MODS:**MULTIORGAN DYSFUNCTION SYNDROME
- **CRP:**C-REACTIVE PROTEIN
- **ERCP:**ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY
- **ARDS:**ACUTE RESPIRATORY DISTRESS SYNDROME
- **BISAP:**BED SIDE INDEX FOR SEVERITY OF ACUTE PANCREATITIS
- **APACHE:**ACUTE PHYSIOLOGY AND CHRONIC HEALTH EVALUATION
- **CSI:**CT SEVERITY INDEX
- **TPN:**TOTAL PARENTRAL NUTRITION
- **SAP:**SEVERE ACUTE PANCREATITIS
- **E2:**SERUM ESTRADIOL
- **SBP:**SYSTOLIC BLOOD PRESSURE
- **DBP:**DIASTOLIC BLOOD PRESSURE
- **LDH:** LACTATE DEHYDROGENASE
- **AST:** ASPARTATE AMINOTRANSFERASE
- **WBC:**WHITE BLOOD CELLS
- **BUN:**BLOOD UREA NITOGEN
- **HCT:**HEMATOCRIT

ABSTRACT

Background and objectives

The present study was undertaken to estimate serum estradiol levels and its co-relation with BISAP (bedside index for severity in acute pancreatitis) score in severe acute pancreatitis.

Methodology

This one year cross sectional study was carried out on a total of 45 consecutive patients with SAP admitted in Medical ICU from January 2014 to December 2014 in the Department of Medicine and gastroenterology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum.

Results

Total no. of cases (n) = 45 were included in our study , patients age ranged from 18 to 92 years and mean age was 38.91 years. Out of the 45 cases, 15 patients expired and 30 patients got discharged. Mean age of expired patients was 42.86 years while mean age of discharged patients was 36.93 years. Among the 45 patients, there were 41 (91.1%) males, and 04 (8.9%) females.

Out of 41 males, 13 expired and 28 got discharged with respective percentage of 31.7% and 68.3%. Out of 4 females, 2 expired and 2 got discharged with respective percentage of 50% for both. P value (0.459) was not significant for sex distribution.

We calculated BISAP score in all our patients. Our study showed a direct correlation between BISAP score and mortality. Out of 15 patients in score 4 category 14 patients expired and one patient improved and got discharged(93.3%).

Score 5 category had only one patient with a mortality percentage of 100% ; with significant p value of <0.001. While there was no mortality in score 2 and 3 categories of BISAP score.

Our results showed that the serum E2 levels in non survivors were significantly elevated at the time of ICU admission and were 3.1 times higher than those of survivors (mean-148 pg/ml Vs 47.7 pg/ml, p < 0.001). In addition, by applying the ROC curve model, we found that sensitivity of 100%, specificity of 96.7%, positive predictive value of 93.8% , Negative predictive value of 100% and an accuracy of 97.78% could be achieved for the prediction of mortality if a serum E2 level of 79.05 pg/ml was chosen as cut off point.

We compared serum E2 levels with BISAP score and found that as the score went on increasing estradiol value was increased, with significant P value <0.001 ; suggestive of reliability of serum E2 levels as an indicator of disease severity.

Conclusion and interpretation

In our study, There was a positive relationship between increasing estradiol values and the increasing BISAP score in SAP patients. Serum estradiol was found to be a early and better predictor for assessing severity regardless of gender.

Keywords

Estradiol, BISAP, SAP, Biomarkers.

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INTRODUCTION

Acute pancreatitis is defined as the inflammation of the pancreas and peripancreatic tissue with multi-organ involvement leading to multi-organ dysfunction syndrome (MODS) which is associated with high mortality[1]. The underlying cause of injury in pancreatitis is the premature activation of pancreatic enzymes within the pancreas, which leads to auto-digestion of pancreatic cells. Once the cellular injury sets in, the inflammatory process causes pancreatic edema, hemorrhage and the end result is necrosis. Inflammatory mediators which are released into circulation leads to systemic complications like bacteremia (due to translocation of gut flora), hemodynamic instability, gastrointestinal hemorrhage, acute respiratory distress syndrome with pleural effusion, renal failure and disseminated intravascular coagulation (DIC).

Acute pancreatitis is divided as mild or severe. The characteristic feature of mild acute pancreatitis is interstitial edema of the gland and minimal or nil organ dysfunction while pancreatic necrosis, severe systemic inflammatory response and often associated with multi-organ failure is seen in severe acute pancreatitis. In patients with mild attack of pancreatitis, the mortality is around 1% and in case of severe attack of pancreatitis, the mortality ranges from 20% to 50%. About one-third of deaths occur in the early phase of attack from multiple organ failure, while deaths occurring late i.e. after first week of onset are as a result of septic complications and multi organ failure.

Most patients of acute pancreatitis recover without developing any complications, the overall mortality rate of pancreatitis is around 2-5%[2,3]. Multiple risk stratification tools for acute pancreatitis are used in practise, but they have limited

clinical usefulness. Previous measures like; the RANSON criteria and modified Glasgow score use data which is difficult to collect at the time of hospitalization. Moreover, both of them require 48hrs to assess the severity, thereby missing early potentially valuable therapeutic window[4]. The APACHE II[5,6] score is the prediction system currently used in on a wide scale in ICU settings which was originally developed for the same. It requires the collection of large number of parameters, some of which may be irrelevant to prognosis.

Henceforth, a simple and accurate clinical scoring system that is bedside index for severity in acute pancreatitis (BISAP) scoring system[7] was developed. This scoring system is used for assessing patients according to their risk of hospital mortality and identifies patients at increased risk of mortality prior to the onset of organ failure as earlier compared to others. Data for BISAP score collected within the first 24 hours of hospitalization. The ability of stratification of the patients early in their course is a major step to improve future management strategies in acute pancreatitis.

Severe acute pancreatitis (SAP) is defined in following criteria[1] :

Early Prognostic Scores:

- RANSON score ≥ 3

Organ Failure:

Any one of following:

- Systolic pressure < 90 mmHg
- PaO2 ≤ 60 mmHg

- Creatinine > 2.0 mg/L after rehydratation
- Gastrointestinal bleeding > 500 cc/24 hr

Local Complications (on CT scan) : any one of following

- Necrosis
- Abcess
- Pseudocyst

BISAP Score:

1. Blood urea nitrogen > 25mg/dl
2. Impaired mental status (Glasgow coma scale score < 15)
3. Systemic inflammatory response syndrome (Presence of more than two of following criteria)

- Pulse >90 bpm

-Respiration >20/min or PaCO2 < 32 mm Hg

-Temperature >38 or < 36 degree Celsius

-WBC count > 12000 or < 4000 cells/cubic mm or > 10% immature neutrophils

4. Age > 60 yrs
5. Pleural effusion (on CT scan or chest x- ray or USG)

Each point on BISAP score is worth 1 point. There is proportionate increase in risk for mortality with the increase in the number of points. BISAP score is a simple, uncomplicated, quick and reliable for assessment of disease severity on admission.

Humans possess peripheral aromatase activity and the resulting ability of converting androgens to estrogens in adipocytes, fibroblasts, and osteoblasts. The peripheral production of estrogens is stimulated by stress. Estradiol (E2) is increased

under conditions of stress like SAP and which enforce exaggerated inflammatory response making it a good and early biomarker for severity in these settings.

Presently there are many scores available to calculate or to define the severity of the SAP but they usually take more time for assessment. By using on admission serum estradiol as severity marker treatment may be started without any delay according to severity which very important for survival of the patient.

OBJECTIVES

1. The objectives of the present study were:

    - To estimate serum estradiol levels and its co-relation with BISAP (bedside index for severity in acute pancreatitis) score in severe acute pancreatitis

REVIEW OF LITERATURE

The ability to asses patients early in their course is a important step to improving future management strategies in acute pancreatitis. The RANSON and modified Glasgow score contain data not routinely collected at the time of hospitalization. In addition both require 48hr to complete, missing a potentially valuable early therapeutic window.

APACHE II was originally developed as an intensive care instrument and requires the collection of a large number of parameters and investigations, some of which may not be relevant to prognosis in acute pancreatitis.

B U Wu et al[7], using classification and regression tree (CART) analysis, a clinical scoring system was developed for prediction of in hospital mortality in acute pancreatitis. The scoring system was derived on data collected from 17,992 cases of acute pancreatitis from 212 hospitals in 2000-2001. The BISAP scoring system was validated on data collected from 18,256 acute pancreatitis cases from 177 hospitals in 2004-2005. The accuracy of the BISAP scoring system for prediction of mortality was measured by the area under the receiver operating characteristic curve (AUC). The performance of the new scoring system was further validated by comparing its predictive accuracy with that of APACHE II.

A new mortality – based prognostic scoring system for use in acute pancreatitis has been derived and validated. BISAP is a simple and accurate method for the early identification within 24 hrs of admission of patients at increased risk for in- hospital mortality.

Vikesh k. singh et al [9], BISAP score was evaluated among 397 cases of acute pancreatitis admitted to their institution between June 2005 and December 2007. BISAP scores were calculated for all cases using data require for score within 24h of presentation. The ability of the BISAP score to predict mortality was evaluated using trend and discrimination analysis. The optimal cutoff score for mortality from the receiver operating curve was used to evaluate the development of organ failure, persistent organ failure, and pancreatic necrosis. Among 397cases, there were 14(3.5%) deaths. There was a statistically significant trend for increasing mortality ($p<0.0001$) with increasing BISAP score. The area under the receiver operating curve for mortality by BISAP score in the prospective cohort was 0.82(95% confidence interval: 0.70, 0.95), which was similar to that of the previously published validation cohort by B U Wu. BISAP score more or equal to 3 was associated with an increased risk of developing organ failure (odds ratio=7.4, 95% confidence interval: 2.8, 19.5), persistent organ failure(odds ratio=12.7, 95% confidence interval:4.7, 33.9) and pancreatic necrosis(odds ratio=3.8, confidence interval:1.8,8.5). Thus the BISAP score represents a easy and fast way to identify patients at risk of increased mortality within 24h of presentation.

ETIOLOGY AND CLASSIFICATION

AP may be classified based on pathology, etiology, severity of disease, or the presence of necrosis. In approximately around 10–20% of patients, etiology is unidentified. Some of these patients may have microlithiasis and/or sphincter of Oddi dysfunction (SOD) as the etiology of AP as odd presentation . With the increasing knowledge and understanding of the role of genetic abnormalities in hereditary idiopathic chronic pancreatitis (CP), it is possible that these abnormalities will be

implicated in idiopathic AP. Furthermore, polymorphisms in inflammatory mediators may influence disease severity.

Clinically, AP is classified as mild or severe disease[10]. Severe acute pancreatitis (SAP) is associated with organ failure and/or local complications, such as necrosis, abscess, or pseudocyst. Approximately 10–20% of patients develop severe disease. Various clinical criteria and scores (e.g., RANSON's or Acute Physiology And Chronic Health Evaluation [APACHE]), serum markers (e.g., interleukin [IL]-6, C-reactive protein, and trypsinogen activation peptide) and imaging modalities (contrast enhanced computed tomography [CT] scan) have been used to predict severity. Complex courses are more common in SAP with mortality rates from 5 to 20%11. In contrast, mild AP is the more frequent presentation and is associated with minimal or temporary organ dysfunction and uneventful recovery.

The presence of pancreatic necrosis is the single best predictor of outcome during AP. Pancreatic necrosis is a diffuse or focal area of nonviable pancreatic parenchyma, typically associated with peripancreatic fat necrosis, which is observed as nonenhanced pancreatic parenchyma on a contrast CT scan. The extent of necrosis can predict morbidity and mortality. Approximately 30% of patients with pancreatic necrosis develop infection within necrosis with a mortality of 6 to 40% and a morbidity of more than 80%.

SPECIFIC ETIOLOGIES

GALLSTONES

Although gallstones are common, they rarely cause pancreatitis. It is estimated that over a 20- to 30 year period, the risk of developing biliary pancreatitis in patients with asymptomatic gallstones is approximately 2%. Small gallstones, particularly

those smaller than 5 mm in size, increase the risk of AP. Additionally, a long common canal at the junction of the bile and pancreatic ducts may increase this risk. The specific mechanism by which gallstones produce pancreatitis is still under evaluation , but most biliary pancreatitis is precipitated by the temporary or persistent obstruction of the ampulla by gallstones. In the majority of patients, these stones pass into the intestine. Bile crystals, like stones, can cause AP. Patients with microlithiasis may present with recurrent "idiopathic" AP. The diagnosis is characterised by transient abnormalities in aminotransferases enzyme levels and the evidence of microscopic crystals in bile. Treatment by cholecystectomy eliminates the risk of recurrence.

ALCOHOL

Alcoholic pancreatitis presents as AP, although in most patients, it occurs in the presence of already established chronic pancreatitis (CP). It is the most common cause of recurrent pancreatitis. The incidence of alcoholic pancreatitis is low (about 5%) in alcohol abusers. This estimate suggests that in addition to alcohol ingestion, other factors, such as genetic background or environmental influences, may affect patient susceptibility. Several major physiological mechanisms may contribute to the development of alcoholic pancreatitis, including abnormal SOD spasm, obstruction of the small ducts by proteinaceous material, and direct toxic effect of alcohol and its metabolites.

HYPERLIPIDEMIA

Hyperlipidemia is a cause of AP and CP. Triglyceride levels greater than 1000 mg/dL are usually required for the development of pancreatitis. The probable disease mechanism is generation of toxic-free fatty acids by the action of lipase on high triglyceride levels in the pancreatic capillary beds, which leads to endothelial damage

with the recruitment of inflammatory cells, thrombosis, and ischemia. Following a bout of AP, patients require lipid lowering medication, as well as treatment of concomitant diabetes and alcohol cessation.

DRUGS

Drugs are a rare cause of AP. Various medications have been implicated in AP. Azathioprine, 6-mercaptopurine, and 2', 3'- dideoxyinosine appear to have an unquestionable association. Other drugs like angiotensin-converting enzyme inhibitors, and tetracycline have a weaker association. The relationship to AP is uncertain in such medications as corticosteroids, aminosalicylic acid, and methyldopa.

ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

AP is the most common complication of endoscopic retrograde cholangiopancreatography (ERCP). Prospective studies have documented an incidence of approximately 5% with most cases being mild pancreatitis. Risk factors include young age, normal pancreatic ducts, operator inexperience, multiple injections of the pancreatic duct with acinarization, pancreatic sphincterotomy, SOD, and biliary or pancreatic sphincter manometry. Several strategies might reduce the incidence of this complication, including the use of protease inhibitors (gabexate mesilate), somatostatin, IL-6 antibodies, and temporary pancreatic duct stenting.

STRUCTURAL

A variety of conditions that obstruct the pancreatic duct chronically or intermittently may cause AP and include SOD, pancreas divisum, and benign and malignant pancreatic duct strictures. SOD is determined by measuring pressures through the sphincter segment at the time of ERCP. This condition is considered when all other possible etiologies have been eliminated, because performing ERCP with

sphincter manometry is also likely to precipitate an attack of AP. Pancreas divisum is a condition in which there is failure of fusion of the dorsal and ventral pancreas during development. Therefore, the secretion of the larger dorsal pancreas drains through the small minor papilla. This common variant occurs in 7% of the population, and very few of these patients develop pancreatitis. In a very small subset, AP may develop. Finally, patients with pancreatic adenocarcinoma may rarely present with unexplained AP, which has led to the recommendation that patients older than 45 years of age with unexplained pancreatitis should undergo an ERCP or endoscopic ultrasonography to evaluate for the possibility of an underlying malignancy

ACUTE BILIARY PANCREATITIS

Gallstones account for between 30 and 50% of AP[12]. It is the most frequent cause of the first AP episode. Most studies exclude patients with microlithiasis; thus, the incidence is likely higher. The wide variation in incidence is noted within and between countries, dependent on the population studied and extent of alcohol use in the community. Gallstone pancreatitis is most common in women between the ages of 50 and 70. However, AP occurs more frequently in males than in females with gallstone disease. The risk for severe disease is similar to that observed for other etiologies, but some studies suggest biliary patients have a higher mortality than alcoholic pancreatitis. This higher mortality may be secondary to the increased risk of cholangitis and the older age of presentation. Biliary pancreatitis may be recurrent if the gallstones are left untreated, although it is not a cause of CP. Recurrence rates are uncertain but may be as high as 30% in the absence of cholecystectomy or biliary sphincterotomy.

ACUTE ALCOHOLIC PANCREATITIS

Excess alcohol intake is the most common etiology of AP in males. Overall, it is the second most common etiology for AP (30%), yet several studies from North America suggest that it may be the most common etiology of AP in the continent. Because alcohol causes recurrent AP, it becomes the predominant etiology when relapses are included in the analysis. Although the incidence of AP is increasing, recent studies do not show any increase in the incidence of alcoholic pancreatitis. Most attacks of acute alcoholic pancreatitis represent an acute attack on CP; however, in most cases, the structural and functional aspects of the pancreas are unknown and the attacks are therefore assumed to be AP. Despite the fact that alcoholic pancreatitis is complicated by severe disease, it is a less common cause of fatal pancreatitis.

OTHER ETIOLOGIES

Other etiologies identified include pancreatic cancer in 1% of cases, post-ERCP in 2–3%, medications in 1%, miscellaneous causes in 2%, and unknown causes in 15–23% of first attacks of AP.

RECURRENT ACUTE PANCREATITIS

Bouts of recurrent AP are most commonly alcohol-related (60%); other etiologies include unknown causes (17%) and untreated gallstones (19%). Recurrent AP appears to be relatively benign and is associated with a low mortality rate.

NATURAL HISTORY

Natural History and Long-Term Outcome. The majority of patients with mild pancreatitis recover uneventfully and once the etiological factor is identified and removed, there are no long-term complications or recurrences. An estimate of 10–

20% of patients with AP develop severe disease and have a complicated hospital course. The incidence of necrosis is between 6 and 20%. Approximately 33% of patients with pancreatic necrosis develop infected necrosis and have the highest mortality and morbidity with nearly 90% of these patients developing failure of at least one organ system[13]. In patients with necrotizing pancreatitis, long-term followup has demonstrated pancreatic ductal changes on ERCP, although the clinical significance of this evidence is uncertain[14]. Following necrosectomy for necrotizing pancreatitis, approximately 50% of patients will develop long-term pancreatic exocrine and endocrine dysfunction, yet most preserve a good overall functional status[15]. The development of pancreatic insufficiency varies with the extent of pancreatic necrosis and resection.

MORTALITY

The mortality of AP is reported in the literature as being between 1.3 and 10%. A range of 2–5% likely represents a true mortality because the higher rates are indicated in studies from referral centers and probably do not include patients with mild disease. Overall, studies suggest a reduction in mortality in the last decade. Gender is not an independent risk factor for severity in AP. When necrotizing pancreatitis is considered, the mortality rate is between 14 and 30%.Approximately half of this mortality is seen in the first 2 weeks. Mortality appears to be influenced by age, etiology (higher in patients with idiopathic, post-ERCP pancreatitis, and gallstone), presence of organ failure on admission and, most importantly, the presence of pancreatic necrosis. Additionally, patients with severe pancreatitis transferred to tertiary care facilities for management have higher mortalities16. Most studies suggest that approximately 10–20% of fatal pancreatitis is missed with the diagnosis only

being made at autopsy. The missed diagnosis appears in patients who present without abdominal pain, with acute respiratory failure or neurological changes, and/or normal serum enzymes or pancreatic imaging.

DIAGNOSIS OF ACUTE PANCREATITIS

Patients with acute pancreatitis (AP) usually present with sudden onset of abdominal pain, nausea, and vomiting. Approximately 80% of patients have interstitial pancreatitis with mild-to-moderate symptoms, and 20% have life-threatening necrotizing disease. Careful clinical assessment and the judicial use of biochemical tests and radiological imaging enables the practitioner to differentiate AP from other causes of acute abdomen and to assess the severity of disease[17-23]

History and Physical Exam

AP is typically characterized by abdominal pain located in the epigatsric or supraumbilical regions, often radiating to the mid-thoracic portion of the back. Pain usually reaches maximum intensity within 20 minutes but may have a more gradual onset. The pain from AP is usually sharp, constant, lasts hours to days, and is severe enough to force the patient to visit the emergency room. In mild AP, the pain may decrease when sitting or leaning forward in comparison to lying flat. Nausea and vomiting with or without low-grade fever are the most commonly associated symptoms.[17,20,21]

A recent history of binge drinking may be frequently elicited in patients with alcohol-induced pancreatitis. The concomitant presence of jaundice and high-grade fever strongly suggests choledocholithiasis as the etiology of AP, complicated by coexistent cholangitis[17-22]. Less commonly, respiratory failure, confusion, and even coma are the main presenting features, which are frequently manifestations of severe

necrotizing pancreatitis. In rare cases, abdominal pain may be absent, leading to a delayed or missed diagnosis[17].

The usual findings on a physical examination are abdominal distension, tenderness, guarding, and absent bowel sounds. Fever associated with AP is generally low grade. High-grade temperature may indicate the development of infected pancreatic necrosis and associated fluid collection or cholangitis, particularly if jaundice is present[17,18,21,22].

Severe acute pancreatitis (SAP) is often complicated by massive loss of fluid into the retroperitoneal spaces. Tachycardia and hypotension are some of the earliest clues for a moderate-to-severe attack of pancreatitis and are markers for significant early depletion of intravascular volume. These may soon progress to hypovolemic shock caused by increased vascular permeability, vasodilatation, and hemorrhage[17]. Tachnypnea and dyspnea are also common in severe pancreatitis, owing to splinting from the subdiaphragmatic inflammatory process, associated pleural effusions, or pulmonary capillary leak syndrome (adult respiratory distress syndrome). Pleural effusions are mainly found on the left side but can be bilateral.

Rare clinical findings include ecchymoses of the umbilicus or flanks, peripheral subcutaneous fat necrosis, and polyarthritis. Classically, dark skin discoloration of the flanks and periumbilical areas because of hemorrhage is described with severe and hemorrhagic pancreatitis; however these physical findings may result from any type of retroperitoneal bleeding[22].

LABORATORY TESTS

The diagnosis of AP is usually suspected based on the appropriate clinical features and is confirmed by laboratory and imaging tests. Leakage of pancreatic enzymes into the circulation is a hallmark of AP. Although amylase and lipase constitute a small fraction of all pancreatic enzymes, they are the easiest and the quickest enzymes to measure. Typically, the elevation of serum amylase in AP is above threefold of the normal values. Amylase levels are usually increased within a few hours of disease onset, but they may be cleared from the serum rather quickly. Serum amylase usually remains elevated for 3–5 days in uncomplicated AP

Causes of Increased Serum Amylase Activity

- Pancreatic diseases
- Acute pancreatitis
- Pancreatic cancer
- Abdominal emergencies
- Acute cholecystitis
- Common bile duct obstruction
- Perforated viscous
- Intestinal ischemia
- Acute appendicitis
- Ruptured ectopic pregnancy and acute salpingitis
- Salivary gland diseases
- Renal insufficiency
- Macroamylasemia
- Diabetic ketoacidosis

- HIV infection/AIDS
- Sphincter Oddi stenosis or spasm
- drugs- morphine

Because many conditions can cause hyperamylasemia, the specificity of elevated serum amylase level is less than 70%. Very high elevations of serum amylase (more than fivefold normal), however, are rarely associated with diseases other than AP. Elevations of three- to fivefold normal are commonly seen in the absence of acute pancreatitis in patients with renal failure, as a result of decreased clearance of the enzyme. Measurements of urinary amylase and the amylase-to-creatinine ratio may be helpful to distinguish AP from other causes of hyperamylasemia, but such measurements are infrequently employed[18-22.]

Serum amylase isoenzyme measurements may improve the diagnostic accuracy of serum amylase alone. In healthy people, less than half of all circulating amylase originates in the pancreas, whereas the remainder is of salivary origin. Serum pancreatic isoamylase (P-isoamylase) accounts for the elevated total serum amylase level in AP and tends to persist for several days. However, pancreatic isoamylase can be elevated in some other gastrointestinal disorders and in renal insufficiency, making it difficult to diagnose AP based on P-isoamylase levels alone without additional diagnostic parameters [18,21,24.] The elevation of serum lipase generally parallels the serum amylase level in AP. However, the serum lipase level often remains elevated longer, making it more useful to diagnose pancreatitis after symptoms have subsided. Lipase is considered more specific than amylase for pancreatic tissue injury, despite that lipase is also produced by numerous other gastrointestinal tissues. Another

potential advantage of lipase is that it is generally not elevated in diabetic ketoacidosis or macroamylasemia[17].

Both amylase and lipase are widely available and are, in general, rapidly available from hospital laboratories. In practice, combining the measurement of serum amylase and lipase somewhat enhances the diagnostic accuracy for AP. A normal amylase or lipase level makes the diagnosis of AP unlikely, except in the presence of hyperlipidemia. Very high levels of serum triglyceride (one of the causes of AP) can interfere with the laboratory assay for both amylase and lipase; dilution of the serum may be necessary in this situation to reliably measure the elevations of amylase or lipase.

In some patients with chronic pancreatitis, acute abdominal pain can be the result of focal acute inflammation of the gland, and serum amylase and lipase levels may remain normal [21,22.] It is important to note that a correlation has not been found between the degree or trend of serum amylase and lipase elevation with the amount of structural damage ofthe pancreas or severity of AP [25.]

Pancreatic enzymes, such as serum trypsin, chymotrypsin, elastase, ribonuclease, and phospholipase A2 have been all reported to be elevated in AP, but assays to measure these enzymes are not readily available for clinical use, and their specificity has notbeen defined [18,21,22,25]. The use of other clinically available laboratory tests may have a role in determining the etiology of AP. For example, elevated bilirubin and hepatic transaminases, particularly alanine aminotransferase more than 80 IU/L should raise the suspicion of gallstone pancreatitis.[17-21]

IMAGING

ULTRASONOGRAPHY

Transabdominal ultrasonography is widely available, relatively inexpensive, and quite safe. Unfortunately, pancreatic imaging by ultrasound has limitations from overlying bowel gas and surrounding fat planes, which tend to be exaggerated in the acutely inflamed pancreas owing to ileus and peripancreatic edema. Thus the sensitivity and specificity of this modality for diagnosing AP is low [17]. Nonetheless, transabdominal ultrasonography is useful in the early stages of AP to search for gallbladder stones or sludge, evaluate for dilation of the common bile duct caused by choledocholithiasis, and analyze for other possible causes of severe abdominal pain.

COMPUTED TOMOGRAPHY SCAN

The computed tomography (CT) scan, particularly when done with helical or multidetector technology, is a valuable tool in the diagnosis and management of AP. However, not every patient with AP requires a CT scan. CT is mainly indicated if the initial diagnosis is in doubt or for prognostic purposes in severely ill patients as in the section on Risk Stratification [20.] The role of CT is both to document the appropriate findings that confirm the diagnosis of AP and to exclude other intraabdominal catastrophes that can mimic AP (e.g., a perforated viscus).

CT scan findings, which support the diagnosis of AP, include diffuse or segmental enlargement of the pancreas, irregularity of the pancreatic contour with obliteration of the peripancreatic fat planes, areas of decreased density within the pancreas, and ill-defined fluid collections in the pancreas or outside the gland in the lesser sac or pararenal spaces. The frequency of these findings varies according to the

severity of pancreatitis, and these findings do not require intravenous administration of contrast material to be identified.

Intravenous contrast-enhanced computed tomography (CECT) is mainly used to differentiate pancreatic necrosis from interstitial pancreatitis or to monitor for pancreatitis complications in selected cases (i.e., to assist in estimating prognosis or managing patients with AP, rather than simply confirming a diagnosis). Normal CT findings have been reported in 24–67% of patients with mild AP [18.]

Controversy exists as to whether intravenous contrast early in the clinical course exacerbates the severity of AP. Although deleterious effects of intravenous contrast have been observed in animal models of experimental pancreatitis, studies in humans have yielded conflicting results [26]. Many authors agree that CECT scans are unneccessary in patients with mild AP and should be reserved for those pateints with a more complicated clinical course. Additionally, early CECT may underestimate the degree of pancreatic necrosis that may develop over time from the disruption of pancreatic microvascular circulation that usually occurs in the first 12–24 hours of SAP [27,28.] At present, it is recommended that CECT be obtained 3–4 days after the onset of SAP for optimal assessment of pancreatic necrosis [24.]

MAGNETIC RESONANCE IMAGING

Currently, magnetic resonance imaging (MRI) has no advantage over CT scan in the management of AP. MRI has a comparable specificity and sensitivity for diagnostic and severity assessment of AP [17,18]. Its cost, availability, and contraindication in patients with metallic implants has limited the application of MRI in AP to date.

ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

Endoscopic retrograde cholangiopancreatography (ERCP) has no role in diagnosing AP. Therapeutic application of ERCP in moderate to severe acute gallstone pancreatitis has been shown by several controlled clinical trials to lower morbidity and mortality when compared to traditional medical treatment alone. ERCP is also utilized in the differential diagnosis and elective treatment of recurrent unexplained pancreatitis secondary to sphincter Oddi dysfunction, pancreatic divisum, and microlithiasis [29-31.]

ENDOSCOPIC ULTRASOUND

The diagnostic role of endoscopic ultrasound (EUS) in AP is still evolving; it is not readily available in all institutions. In recent studies, the immediate application of EUS for suspected biliary AP may aid in the diagnosis of gallstone pancreatitis, thereby helping to triage patients for therapeutic ERCP with endoscopic sphincterotomy and stone removal [32].

RISK STRATIFICATION IN ACUTE PANCREATITIS

Early evaluation of AP severity is essential to allow the clinician to predict the patient's clinical course, estimate prognosis, and determine the need for intensive care unit admission. Severe pancreatitis can be defined by various systems that predict complications and mortality or by the development of the complication itself. Thus, there is a difference between a predictive system that suggests complications may develop and the actual development of a complication. This section focuses on methods to predict morbidity and mortality. Severe pancreatitis can be predicted by clinical criteria, multiple factor scoring systems, serum markers, and radiographic features. The ability of a seasoned clinician's ability to detect severe pancreatitis is

similar to the accuracy of the multiple factor scoring systems. Several of these scoring systems have been developed to assist the clinician in the assessment of the severity of AP.The most commonly used systems are the RANSON criteria, the modified Glasgow scoring system, and the Acute Physiology And Chronic Health Evaluation II (APACHE II) [18,24,32-35]

RANSON Criteria and the Modified Glasgow System: They rely on a collection of clinical and biochemical variables measured within the first 48 hours of admission. Clearly, from looking at these systems, many of the variables are factors that any clinician would be attuned to in managing a critically ill patient and the scoring systems merely place these variables within a numerical framework. Using these systems, it is only possible to predict severity after 48 hours have passed. Higher RANSON or Glasgow scores predict severe disease with reasonable sensitivity. Mortality is less than 5% in patients with RANSON score of 0, in comparison to 10% for those with a criteria of 3–5, and 60% for those with a RANSON score greater than 6. Thus, many patients with higher RANSON scores do not die and, in fact, do not develop organ failure or other complications. The same is true for the modified Glasgow scoring system. Therefore, the RANSON and modified Glasgow scoring systems lack specificity. It should also be noted that there are separate RANSON scoring systems for alcohol-induced and biliary pancreatitis, and the total score cannot be calculated unless all factors are measured after 48 hours of observation.

The most important roles of the RANSON and Glasgow scoring may be to exclude severe disease. A Glasgow or RANSON score of 0 or 1 virtually guarantees that complications will not develop and that mortality will be negligible. A second

important use of these scoring systems is for clinical research, in characterizing disease severity for comparison between studies.

VARIABLES OF THE RANSON CRITERIA AND MODIFIED GLASGOW SYSTEM

RANSON Criteria

For Acute Non-Gallstone Pancreatitis

Upon admission:

1. Age >55 years
2. WBC >16,000/mm3
3. Glucose >200 mg/dL
4. LDH >350 IU/L
5. AST >250 IU/L

Within 48 hours:

1. Drop in HCT >10%
2. Serum Ca <8 mg/dL
3. Base deficit >4 mEq/L
4. Increase BUN >5 mg/dL
5. Fluid deficit >6 L
6. Arterial PO2 <60 mmHg

For Acute Gallstone Pancreatitis

Upon admission:

1. Age >70 years
2. WBC >18,000/mm3
3. Glucose >220 mg/dL

4. LDH >400 IU/L
5. AST >440 IU/L

Within 48 hours:

1. Drop in HCT >10%
2. Serum Ca <8 mg/dL
3. Base deficit >5 mEq/L
4. Increase BUN >2 mg/dL
5. Fluid deficit >6 L
6. Arterial PO2 <60 mmHg

- Modified Glasgow System
- Arterial PO2 <60 mmHg
- Serum albumin <3.2 g/dL
- Serum Ca <8 mg/dL
- WBC >15,000/mm3
- AST >200 IU/L
- LDH >600 IU/L
- Glucose >180 mg/dL
- BUN >45 mg/dL

The APACHE II scoring system is considered more specific and accurate when compared to clinical assessment and RANSON/modified Glasgow system. The APACHE II may be applied at any time point in the course of disease, which is an advantage over the RANSON and Glasgow criteria. The APACHE II system is quite complex [25], making it unwieldy for everyday clinical use. Many free downloadable

programs for PDA use are available on the Web, which has markedly improved the ease in using the APACHE II scoring system.

Predicted SAP is defined by a RANSON score of 3 or greater or an APACHE II score of 8 or Greater [24,25.] Actual SAP is defined by the presence of organ failure or local pancreatic complications (e.g., necrosis, infected necrosis, pseudocyst, and abscess).

CT has also become routinely used in the prediction and determination of disease severity. The initial CT grading system, which did not require intravenous contrast administration, was developed by Balthazar and RANSON [36]. However, using CT alone also has a relatively high false-positive rate (i.e., many patients with grade C and even D pancreatitis recover without developing organ failure or dying). Combining the CT grading system with RANSON prognostic signs further improves the prognostic capacity when compared to either system alone. Patients with grade D or E are almost certain to develop complications, and they have a significantly increased risk of mortality, and this risk is augmented by the coexistence of a high RANSON score. Those patients with grade C pancreatitis and a RANSON score less than 3 routinely do well, whereas those with grade C pancreatitis and a RANSON score more than 3 are much more likely to develop complications and/or die. A grade of A or B strongly predicts an uncomplicated outcome [17,36]. These grading systems are based on non-CECT scans. CECT can be used to determine the presence of pancreatic necrosis. Interstitial pancreatitis (the absence of necrosis) is defined by homogeneous and uniform intravenous contrast enhancement of the pancreas, which requires rapid scanning over the pancreas timed to the infusion of intravenous contrast. Necrosis is defined by inhomogeneous enhancement with intravenous contrast, especially when

large areas of the pancreas are entirely devoid of enhancement. Pancreatic necrosis per se is not always associated with other clinical features of severe disease (e.g., organ failure or infected necrosis), but the presence of necrosis markedly increases the chance of developing these severe clinical markers. Particularly, pancreatic necrosis puts patients at risk for infection of the devitalized tissue, one of the most severe complications of AP. CT scans with intravenous contrast enhancement is our only method currently available to identify necrosis.

Given that the multiple factor scoring systems are complex and that CT scans are expensive, there has been continued interest in identifying simpler or less expensive methods to predict severity. Several clinical and serum markers of disease severity have been proposed, which include routine laboratory tests and novel markers of disease severity. Despite the diagnostic importance of elevated serum amylase and lipase in AP, numerous studies have demonstrated that elevated levels of these enzymes have no prognostic value in AP [18,24,25]. This is the reason why they are excluded in any AP severity scoring system. Hemoconcentration more than 44% at presentation has been demonstrated by several investigators to be a reasonably accurate early marker that predicts pancreatic necrosis and organ failure [37-39]. In contrast, Whitcomb et al. showed that an admission hematocrit of 40% or below predicts a low risk of pancreatic necrosis and may reduce the need for diagnostic CT scans [40]

Computed Tomography Grading System

Grade A: Normal findings

Grade B: Focal or diffuse pancreatic enlargement

Grade C: Inflammation of the pancreas and pancreatic fat

Grade D:Peripancreatic fluid collection in single location (within anterior para-renal space)

Grade E: Two or more fluid collections or the presence of peripancreatic gas

More novel serum tests have also been evaluated. C-reactive protein (an acute-phase reactant) is cheap, widely available, and commonly used in Europe as a measure of severity. A level of 150 mg/L of C-reactive protein has been proposed as a criterion for distinguishing mild AP from SAP [25.] Other markers, such as trypsinogen activation peptide, interleukin-6, and polymorphonuclear elastase, have been shown in research studies to be of value to predict severe necrotizing pancreatitis, but commercial assays are not yet available for clinical use [18-23.] Clinical or demographic features may also predict disease severity. Obesity has been shown in several studies to be a risk factor for the severe outcome of AP, and it is associated with an increased risk of mortality [25.] Advanced age and comorbid diseases are also risk factors for morbidity and mortality from AP. Other clinical parameters like hypovolemic shock, massive pleural effusion, prolonged hypoxia, and body echymosis are indicative of a complicated course and a higher risk of mortality [17.]

Many steps have already been taken to guide the clinician's goal of predicting the severity of AP. The ability to accurately predict outcome would allow the improved use of intensive and intermediate care unit beds and would allow specific therapy (once available) to be directed at those patients most likely to benefit. However, the ideal grading system or the predictive marker of choice does not yet exist. Careful and repeated clinical evaluation by skillful clinicians remains an important part of detecting complications early. Multiple factor scoring systems are useful adjuncts but remain complex, difficult to use, and all have a high false-positive

rate. CT scans are widely used and seem to provide the best addition to clinical assessment, both to confirm the diagnosis and/or rule out alternative diagnoses and estimate the disease severity.

BISAP SCORE

The ability to stratify patients early in their course is a major step to improving future management strategies in acute pancreatitis. The RANSON and modified Glasgow score contain data not routinely collected at the time of hospitalization. In addition both require 48hr to complete, missing a potentially valuable early therapeutic window. APACHE II was originally developed as an intensive care instrument and requires the collection of a large number of parameters, some of which may not be relevant to prognosis in acute pancreatitis.

B U Wu et al[7], using classification and regression tree (CART) analysis, a clinical scoring system was developed for prediction of in hospital mortality in acute pancreatitis. The scoring system was derived on data collected from 17,992 cases of acute pancreatitis from 212 hospitals in 2000-2001. The BISAP scoring system was validated on data collected from 18,256 acute pancreatitis cases from 177 hospitals in 2004-2005. The accuracy of the

BISAP scoring system for prediction of mortality was measured by the area under the receiver operating characteristic curve (AUC). The performance of the new scoring system was further validated by comparing its predictive accuracy with that of APACHE II. A new mortality – based prognostic scoring system for use in acute pancreatitis has been derived and validated. BISAP is a simple and accurate method for the early identification of patients at increased risk for in- hospital mortality.

Vikesh K. Singh et al [9], BISAP score was evaluated among 397 consecutive cases of acute pancreatitis admitted to their institution between June 2005 and December 2007. BISAP scores were calculated on all cases using data within 24h of presentation. The ability of the BISAP score to predict mortality was evaluated using trend and discrimination analysis. The optimal cutoff score for mortality from the receiver operating curve was used to evaluate the development of organ failure, persistent organ failure, and pancreatic necrosis. Among 397 cases, there were 14(3.5%) deaths. There was a statistically significant trend for increasing mortality ($p<0.0001$) with increasing BISAP score. The area under the receiver operating curve for mortality by BISAP score in the prospective cohort was 0.82(95% confidence interval: 0.70, 0.95), which was similar to that of the presentation validation cohort by B U Wu.

BISAP score more or equal to 3 was associated with an increased risk of developing organ failure (odds ratio=7.4, 95% confidence interval: 2.8, 19.5), persistent organ failure (odds ratio=12.7, 95% confidence interval: 4.7, 33.9) and pancreatic necrosis (odds ratio=3.8, confidence interval:1.8, 8.5). Thus the BISAP score represents a simple way to identify patients at risk of increased mortality and the development of intermediate markers of severity within 24 hrs of presentation Individual components of the BISAP scoring system

- BUN > 25 mg/dl
- Impaired mental status (Glasgow Coma Scale Score < 15)
- SIRS- SIRS is defined as two or more of the following:
    (1) Temperature of < 36 or > 38 ° C
    (2) Respiratory rate > 20 breaths/min or $PaCO_2$ < 32 mm Hg

(3) Pulse > 90 beats/min

(4) WBC < 4,000 or >12,000 cells/mm3 or >10% immature bands

Age > 60 years

Pleural effusion detected on imaging

One point is assigned for each variable within 24 hrs of presentation

BISAP, bedside index for severity in acute pancreatitis; SIRS, systemic inflammatory response syndrome.

Serum Estradiol

Estradiol, or more precisely, 17β-estradiol, is a human sex hormone and steroid, and the primary female sex hormone. It is important in the regulation of the estrous and menstrual female reproductive cycles. Estradiol is essential for the development and maintenance of female reproductive tissues[43]. While estrogen levels in men are lower compared to women, estrogens have essential functions in men as well.

Estradiol or oestradiol (American or British English usages), derives from estra-, Gk. οστρος (oistros, literally meaning "verve or inspiration")[44] and -diol, a chemical name and suffix indicating that this form of steroid and sex hormone is a type of alcohol bearing two hydroxyl groups.

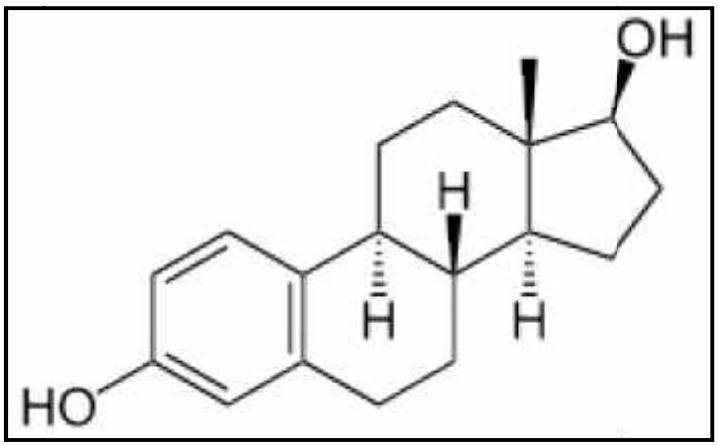


FIG 1: Structure of estradiol

Estradiol is produced especially within the follicles of female ovaries, but also in other endocrine (i.e., hormone-producing) and non-endocrine tissues (e.g., including fat, liver, adrenal, breast, and neural tissues). Estradiol is biosynthesized from progesterone (arrived at in two steps from cholesterol, via intermediate pregnenolone). One principle pathway then converts progesterone to its 17-hydroxy-derivative, and then to androstenedione via sequential cytochrome P450-catalyzed oxidations. Action of aromatase on this dione generates estrone, and action of a dehydrogenase on this gives the title compound, 17β-estradiol.

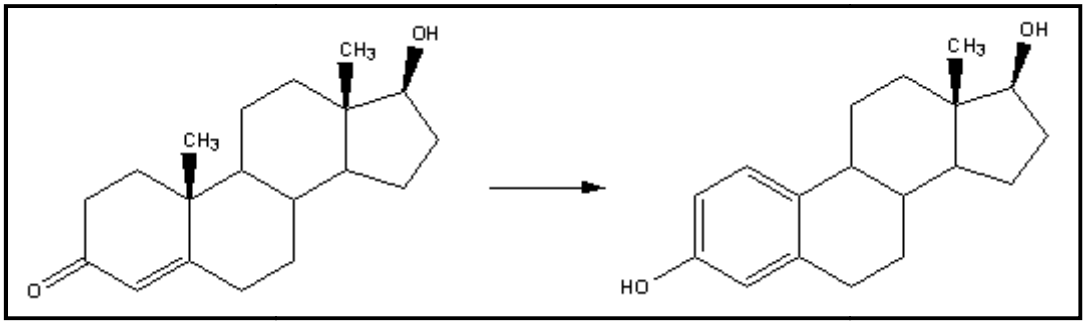


FIG 2: Conversion of testosterone to estradiol

Conversion of testosterone to estradiol; Estradiol like other steroids, is derived from cholesterol. After side chain cleavage and using the delta-5 or the delta-4 pathway, androstenedione is the key intermediary. A fraction of the androstenedione

is converted to testosterone, which in turn undergoes conversion to estradiol by an enzyme called aromatase. In an alternative pathway, androstenedione is aromatized to estrone, which is subsequently converted to estradiol[45]

During the reproductive years, most estradiol in women is produced by the granulosa cells of the ovaries by the aromatization of androstenedione (produced in the theca folliculi cells) to estrone, followed by conversion of estrone to estradiol by 17β-hydroxysteroid dehydrogenase. Smaller amounts of estradiol are also produced by the adrenal cortex, and (in men), by the testes.

Estradiol is not produced in the gonads only, in particular, fat cells produce active precursors to estradiol, and will continue to do so even after menopause.[46] Estradiol is also produced in the brain and in arterial walls, though it cannot be readily transferred from the circulatory system into the brain.[47] However, as one of the two active metabolites of testosterone in males (the other being dihydrotestosterone), it can be produced from this hormone within the brain.

The source of elevated serum estrogens in critically ill patients is unknown but is thought to be related to increased peripheral conversion of androgens to estrogens via aromatase activity [48-53.] These peripheral sites of aromatization account for the majority of estrogens in men and postmenopausal women [48] and may be an important source of estrogens during critical illness. A recent study of elective cardiac surgery patients demonstrated that the elevation in estrogens present postoperatively was due to increased peripheral aromatase activity and not related to reduced clearance[52.] A nonspecific increase in the production of all sex hormones via the hypothalamic-pituitary axis seems unlikely because luteinizing hormone and follicle-stimulating hormone levels are suppressed in critically ill patients and other precursor hormones

seem to be low[54.] Although few data are available regarding estrogen metabolism during critical illness, the predominant pathways of estrogen clearance seem to be maintained unless severe hepatic failure is present [55.]

Unlike gonadal or brain aromatase, the peripheral aromatase promoter is specifically stimulated by tumor necrosis factor-α and class 1 cytokines in the presence of glucocorticoids, thus increasing estrogen synthesis in settings of stress [51,56.] In light of the known immunomodulating properties of E2, this non–sex-dependent increased conversion could contribute to the divergence of results obtained between animal models and human observational studies. In addition, this peripheral aromatization, as the main source of estrogens in men and postmenopausal women, provides the rationale for our finding that elevated serum E2 was associated with both age and body mass index. An important feature of aromatase expression, specifically in adipose tissue, is that it increases with advancing age [48.] One possible explanation is that cytokines such as IL-6 are elevated in older patients, at least in serum [57.] Likewise, aromatase activity is known to increase with increasing adiposity, also likely due to increased levels of cytokines [48.] Humans possess peripheral aromatase activity and the resulting ability to convert androgens to estrogens in adipocytes, fibroblasts, and osteoblasts. This peripheral production of estrogens stimulated by stress. Estradiol (E2) would be increased under conditions of stress like SAP and which enforce exaggerated inflammatory response making it a good and early biomarker for severity in these settings settings and its comparison with BISAP score will standardized it .

Reference ranges for serum estradiol			
Patient type	**Lower limit**	**Upper limit**	**Unit**
Adult male	50	200	pmol/L
	14	55	pg/mL
Adult female (follicular phase, day 5)	70	500	pmol/L
	110	220	
	19 (95% PI)	140 (95% PI)	pg/mL
	30 (90% PI)	60 (90% PI)	
Adult female (preovulatory peak)	400	1500	pmol/L
	110	410	pg/mL
Adult female (luteal phase)	70	600	pmol/L
	19	160	pg/mL
Adult female - free (not protein bound)	0.5	9	pg/mL
	1.7	33	pmol/L
Post-menopausal female	N/A	< 130	pmol/L
	N/A	< 35	pg/mL

FIG 3 : Reference ranges for serum estradiol

The estradiol produced by male humans, from testosterone, is present at serum levels roughly comparable to postmenopausal women (14-55 versus <35 pg/mL, respectively).

In a study done in 2012 at china medical university hospital, department of trauma and emergency, Taiwan , ROC.of the 62 who enrolled in to the study who are already diagnosed as severe acute pancreatitis as per criteria proposed by the international Atlanta Symposium on Acute pancreatitis in 1992 . Out of that serum estradiol was significantly elevated in nonsurvivors (39 vs 206 pg/mL , $p < 0.001$)

compared to survivors. The estradiol level was the best single-variable predictor of mortality followed by MODS, APACHE2 score.[58]

Study done at Division of Trauma and Surgical Critical Care and the Department of Surgery,Vanderbilt University Medical Center, Nashville, TN; and the Department of Surgery, University of Virginia Health System, Charlottesville, VA in 2008 ; A total of 301 adult critically ill or injured surgical patients remaining in the intensive care unit for ≥48 hrs were enrolled; in that group of patients Estradiol was significantly higher among nonsurvivors ($p < .001$).[59]

Other study done at Division of Trauma & Surgical Critical Care, Department of Surgery, Vanderbilt University Medical Center, Nashville, Tennessee. It was found that There was no difference in mortality rates between the sexes and the serum estradiol concentration was significantly elevated in non-survivors regardless of sex.[60]

METHODOLOGY

The present study was conducted in the Department of Medicine and Gastroenterology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on patients with severe acute pancreatitis during the period of January 2014 to December 2014.

Study design

The study design was one year cross sectional study.

Study period and duration

The present one year study was conducted during the period of January 2014 to December 2014.

Method of collection of data

Source of Data

This study was conducted on patients admitted with acute pancreatitis in Medical Intensive Care Unit (MICU) at KLES Dr Prabhakar Kore Hospital and Medical Researcgh Centre, Belgaum. The MICU is equipped with a split level air conditioning system having nurse patient ratio of 1:3 for ventilated patients. It has facilities for conventional ventilatory support and rigorous monitoring of all critically ill patients.

Sample size and sampling method

A total of 45 patients admitted with acute pancreatitis during the study period at MICU, KLES Dr Prabhakar Kore Hospital and Medical Research Centre, Belgaum were included in the study.

Selection criteria

Inclusion Criteria

- All MICU patients above the age of 18 years of either gender admitted with acute pancreatitis were included in the study.

Exclusion Criteria:

1. Women on OC pills
2. Patient who is known case of
3. liver cirrhosis
4. Polycystic ovarian disease
5. Endometrial carcinoma
6. Adrenal hyperplasia

Severe acute pancreatitis diagnosed by Atlanta criteria as well as BISAP score on admission :

- **Severe Acute Pancreatitis Criteria :**

Early Prognostic Scores :

- RANSONscore ≥ 3

Organ Failure : any 1 of following :

- Systolic pressure < 90 mmHg
- PaO2 ≤ 60 mmHg
- Creatinine > 2.0 mg/L after rehydratation
- Gastrointestinal bleeding > 500 cc/24 hr

Local Complications (on CT scan) : any 1 of following

- Necrosis
- Abcess
- Pseudocyst

BISAP score

Individual components of the BISAP scoring system

- BUN > 25 mg/dl
- Impaired mental status (Glasgow Coma Scale Score < 15)
- SIRS-SIRS is defined as two or more of the following:

(1) Temperature of < 36 or > 38 ° C

(2) Respiratory rate > 20 breaths/min or PaCO2 < 32 mm Hg

(3) Pulse > 90 beats/min

(4) WBC < 4,000 or >12,000 cells/mm3 or >10% immature bands

- Age > 60 years
- Pleural effusion detected on imaging

One point is assigned for each variable within 24 hrs of presentation BISAP, bedside index for severity in acute pancreatitis; SIRS, systemic inflammatory response syndrome.

Procedure

The study was approved by the Institutional Ethics Committee of Jawaharlal Nehru Medical College, Belgaum. Patients Admitted in MICU under the Department of Medicine and Gastroenterology at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum were evaluated based on diagnostic criteria for Acute severe pancreatitis atlanta criteria and BISAP score.The selected patients were briefed

about the nature of the study and a written informed consent was obtained (Annexure–I).

Demographic data like gender and age were collected along with relevant history and recorded on predesigned and pretested proforma (Annexure-II). A thorough clinical examination was conducted and the findings were also recorded.

All relevant data from patient's medical records, bed-side flow sheets including gender, age, admission diagnosis were noted. History of preexisting diseases like Diabetes Mellitus, Hypertension, Stroke, Ischaemic Heart Disease, and previous admission to hospital and present symptomatology was listed and detailed physical examination was done. Details of medical interventions were recorded.

Blood sample will be collected for Complete Blood Count, Liver function tests, Renal function tests, Pancreatitis diagnostic panel (amylase, lipase, LDH etc) HIV ELISA, and Serum Estradiol, within 24 hours of admission. Appropiate cultures will be taken. Chest X-ray and other imaging modalities will be done as required.

SAMPLE COLLECTION

Approximately, 20ml of blood was collected from the peripheral venous site.

The venepuncture site was disinfected with surgical spirit (70% alcohol) rubbing vigorously and allowed to dry. This was followed by application of Povidone iodine in concentric circles over the site and allowed to dry for at least I minute. About 20 ml of blood was collected, out of which 15ml was inoculated aseptically into blood culture bottle, 2ml was collected in sterile bottle to separate serum for Estradiol , 1ml of blood was collected in a sterile bottle containing the anticoagulant

EDTA for estimation of complete blood count, and 2ml for renal and liver function tests as well as pancreatitis panel.

Blood culture

About 15ml of blood was drawn aseptically and inoculated into a blood culture bottle. After inoculation, the blood culture bottles were incubated at 37 degree centigrade under aerobic conditions in the incubator for 7 days. The first subculture was done after 24 hours of incubation, the second on the third day and final on the seventh day.

Subcultures were done on to chocolate agar, 5% sheep blood agar and Mac Conkey agar plates. The inoculated plates were incubated aerobically in the incubator for 37 degree centigrade and the plates were observed for growth. The growth was identified by colony characteristics, grams stain and biochemical tests.

Cultures which did not yield any growth following three subcultures were reported negative at the end of 7 days.

ESTRADIOL

Estradiol level analysis was done using enzyme linked immunoflourescence assay. Other hematological tests

A drop of EDTA blood was taken on a clean dry slide and a thin tongue shaped smear was made, air dried and stained with Leishman stain. The Total count, absolute neutrophil count and band cell ratio were calculated as per standard hematological methods. Other tests were performed as and when required using standardized methods.

Statistical analysis

The data obtained was tabulated on Excel spread sheet (Annexure IV). The data was expressed as rates, ratios and percentages. The continuous variables were expressed as mean and standard deviation (SD). The data will be compared using unpaired‘t’ test. A probability value (p value) of less than or equal to 0.05 was considered as statistically significant.

Significance is assessed at 5% level of significance.

Chi-square/Fisher Exact test has been used to find the significance of study parameters on categorical scale between two groups.

Diagnostic statistics viz. Sensitivity, Specificity, PPV, NPV, was computed and 90% confidence interval computed in the study.

RESULTS

This cross sectional study was conducted in the department of Medicine and Gastroenterology of KLES Dr. Prabhakar Kore Hospital and Research Centre over a period of one year from January 2014 to December 2014. The blood samples taken from 45 patients meeting the inclusion and exclusion criteria constituted the material for study.

Descriptive Statistics for age (yrs)

Total no. of cases (n) = 45, minimum age was 18 years and maximum age was 92 years, mean age was 38.91 years

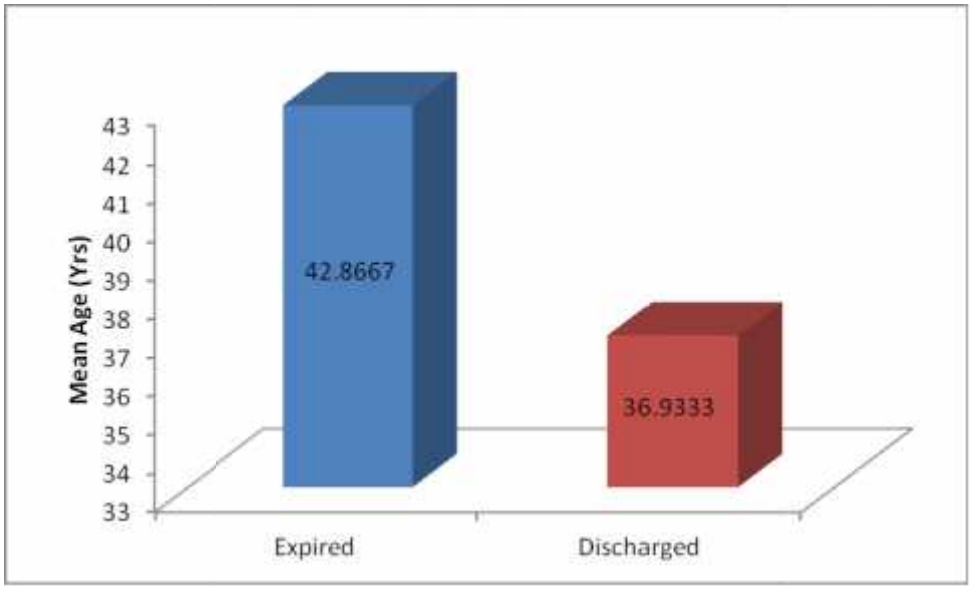
Table 1: Age distribution

N	Minimum Age in years	Maximum Age in years	Mean age in years
45	18.00	92.00	38.9111

Table 2: Distribution of cases according to age (n=45)

Outcome	N	Mean of age in years	p-value
Expired	15	42.8667	0.218
Discharged	30	36.9333	

Graph 1: Distribution of cases according to Age



Out of 45 patients, 15 expired and 30 got discharged. Mean age of expired patients was 42.86 years while mean age of discharged patients was 36.93 years.

Distribution of cases according to sex (n=45)

Frequency Table

Sex	Frequency	Percent
Male	41	91.1
Female	4	8.9
Total	45	100.0

Among the 50 patients, there were 41 (91.1%) males, and 04 (8.9%) females.

Graph 2: percentage of patients got discharged and expired

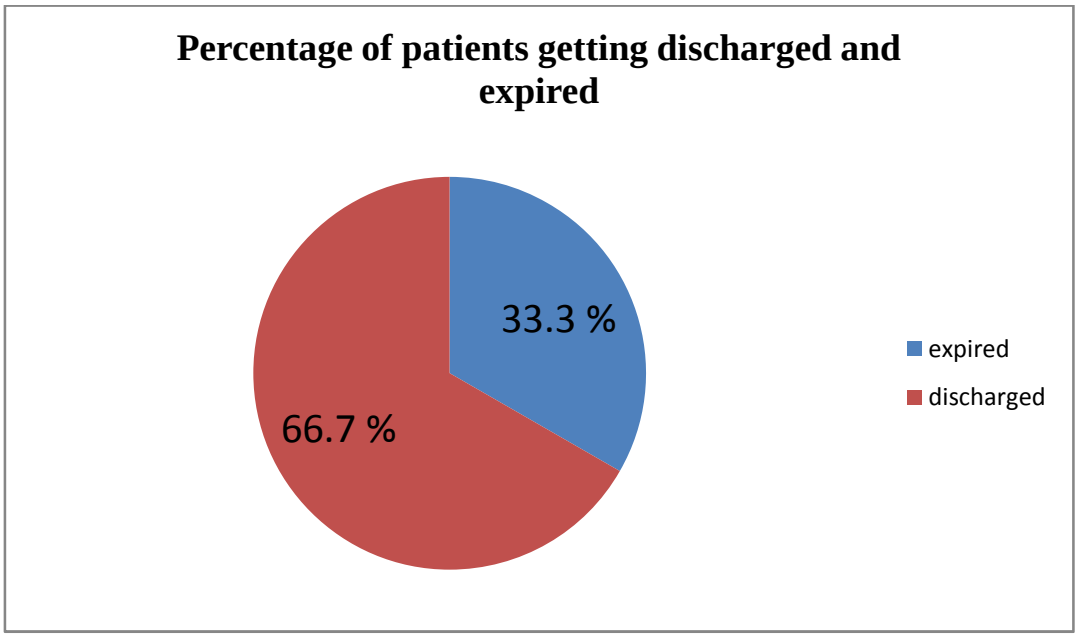


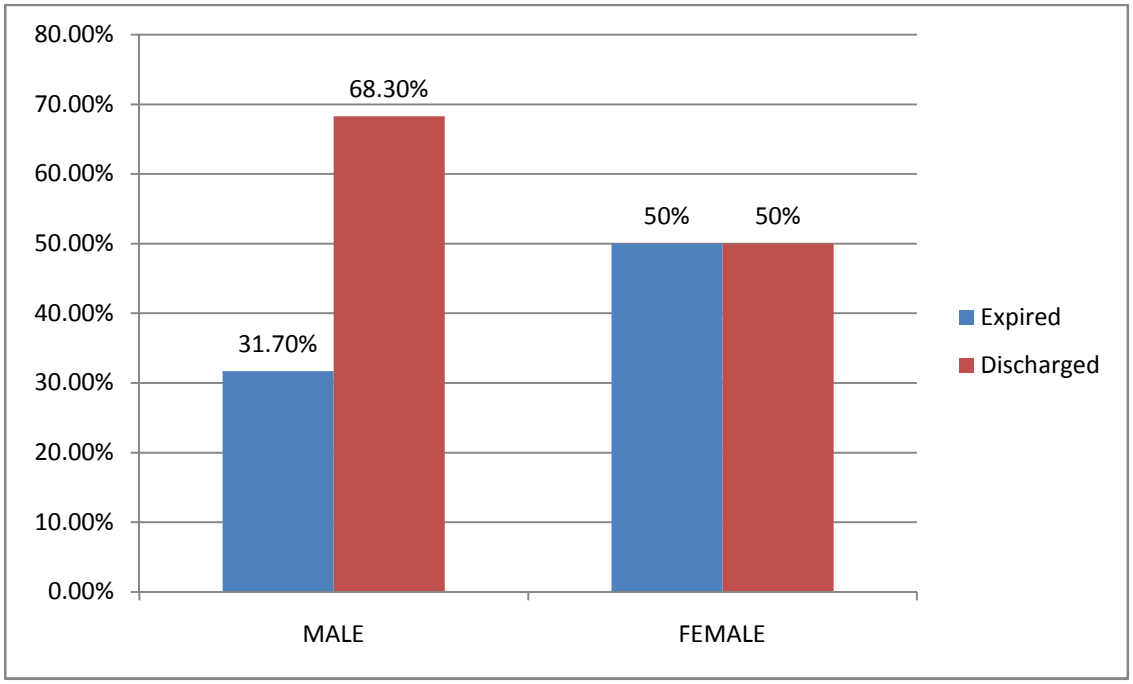
Table 3: Distribution of cases regarding outcome (n=45)

Outcome	Frequency	Percent
Expired	15	33.3
Discharged	30	66.7
Total	45	100.0

Table 4: Distribution of cases according to sex regarding outcome

Sex	Outcome		
	Expired	Discharged	Total
Male	13	28	41
	31.7%	68.3%	100.0%
Female	2	2	4
	50.0%	50.0%	100.0%
Total	15	30	45
	33.3%	66.7%	100.0%

Graph 3: Distribution of sex



	Value	p-value
Pearson Chi-Square	0.549	0.459

Out of 41 males 13 expired and 28 got discharged with respective percentage of 31.7% and 68.3%. Out of 4 females 2 expired and 2 got discharged with respective percentage of 50% for both. P value (0.459) was not significant for sex distribution.

Graph 4: Distribution of sex regarding outcome

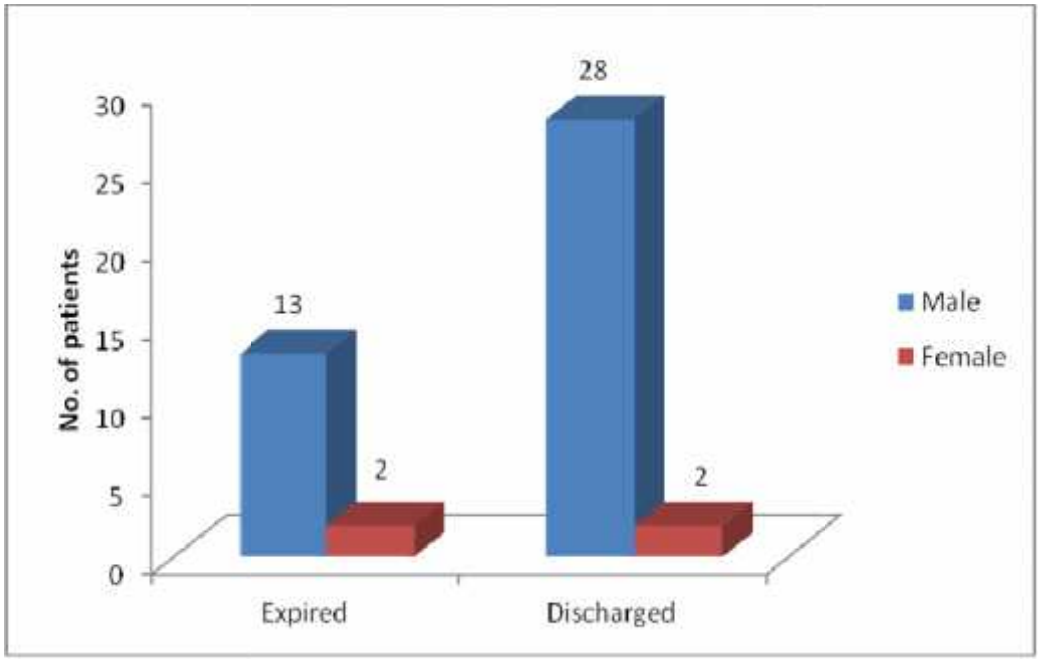


Table 5: Relation of RANSON score and outcome

RANSON Score	Outcome		
	Expired	Discharged	Total
3	1	28	29
	3.4%	96.6%	100.0%
4	1	0	1
	100.0%	0%	100.0%
5	13	2	15
	86.7%	13.3%	100.0%
Total	15	30	45
	33.3%	66.7%	100.0%

	Value	p-value
Pearson Chi-Square	32.855	<0.001

As shown in the above tables there was a direct correlation between RANSON score and mortality; maximum mortality was observed in patients with score 5 which was for 13 patients (86.7%) with significant p value of <0.001

Graph 5: RANSON score and outcome

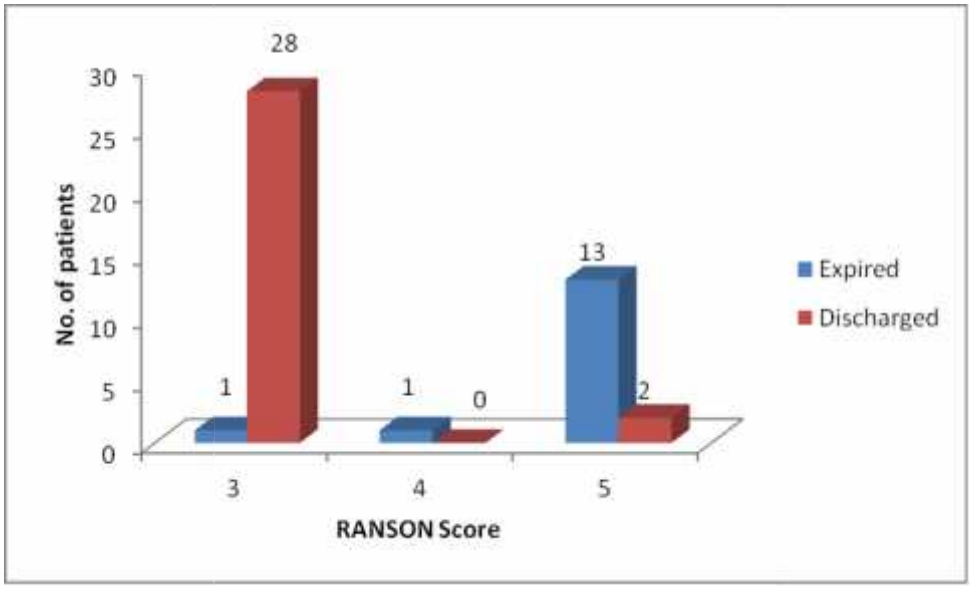


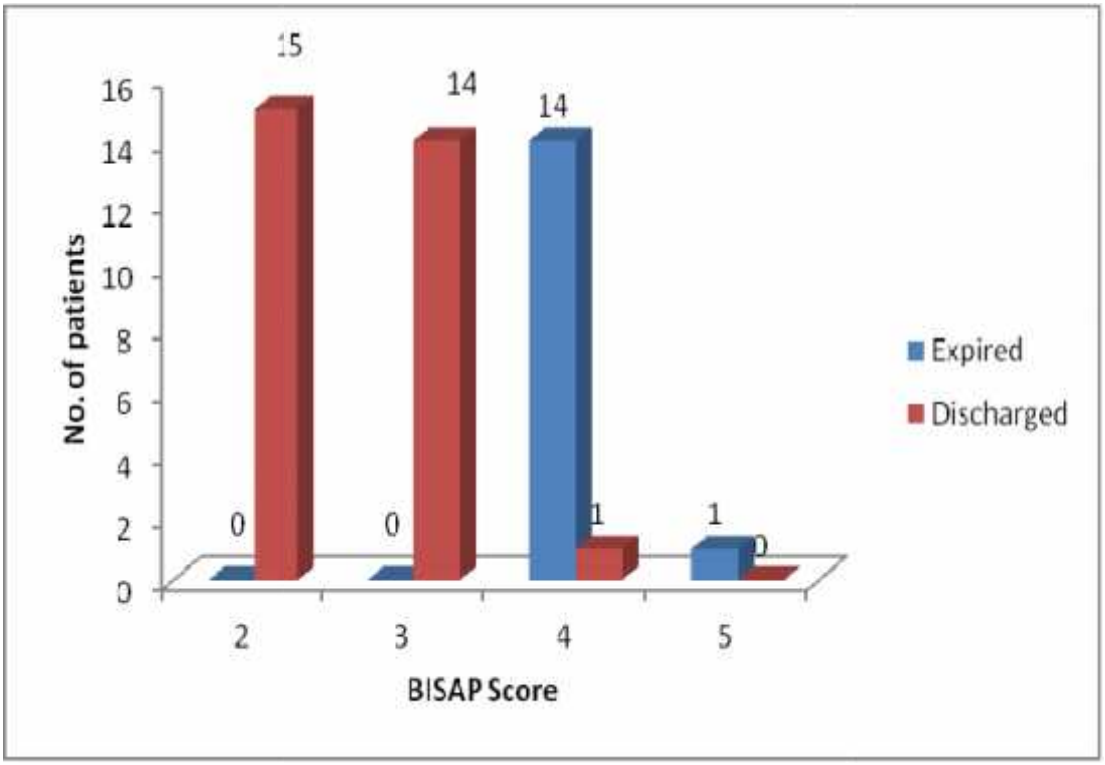
Table 6: Relation of BISAP score and outcome

BISAP Score	Outcome		
	Expired	Discharged	Total
2	0	15	15
	0%	100.0%	100.0%
3	0	14	14
	0%	100.0%	100.0%
4	14	1	15
	93.3%	6.7%	100.0%
5	1	0	1
	100.0%	0%	100.0%
Total	15	30	45
	33.3%	66.7%	100.0%

	Value	Exact p-value
Pearson Chi-Square	40.800	<0.001

As shown in the above tables there was a direct correlation between BISAP score and mortality; maximum mortality was observed in patients with score 4 and 5. Out of 15 patients in score 4 category 14 patients expired and one patient improved and got discharged (93.3%) , Score 5 category had only one patient with mortality percentage of 100% ; with significant p value of <0.001. While there was no mortality in score 2 and 3 categories of BISAP score.

Graph 6 : BISAP score and outcome



ROC Curve to find out cutoff of Serum Estradiol for outcome

Outcome	No. of patients
Expired	15
Alive	30

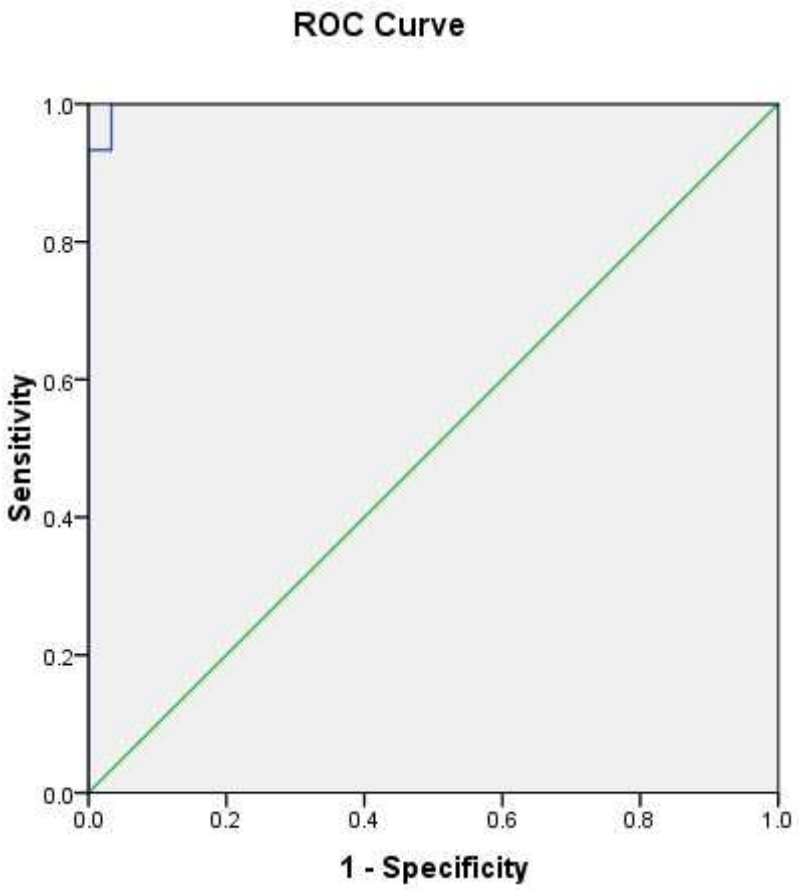


Table 7 : Area under the curve

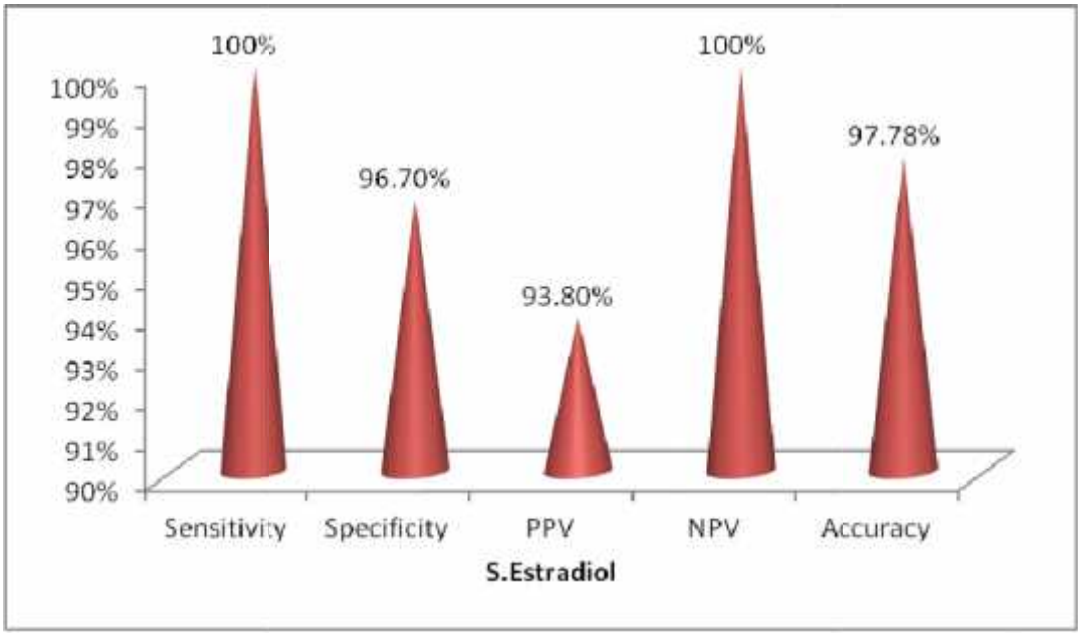
Area Under the Curve				
			Asymptotic 95% Confidence Interval	
Area	Std. Error	p-value	Lower Bound	Upper Bound
0.998	0.004	<0.001	0.990	1.005

By the ROC curve cut off value for serum estradiol was 79.05.

Table 8: Sensitivity, Specificity, PPV, NPV and Accuracy of serum estradiol

Sensitivity	Specificity	PPV	NPV	Accuracy
100%	96.7%	93.8%	100%	97.78%

Graph 7 : Sensitivity, Specificity, PPV, NPV and Accuracy of serum estradiol



Sentivity of serum estradiol for detection of mortality was 100 % ;

Speficity of serum estradiol for detection of mortality was 96.70 % ;

PPV of serum estradiol for detection of mortality was 93.80 % ;

NPV of serum estradiol for detection of mortality was 100% ;

Accuracy of serum estradiol for detection of mortality was 97.78 % .

Table 9 : Cut off value of serum estradiol

S_Estrediol	Outcome		
	Expired	Discharged	Total
>=79.05	16	0	16
<79.05	0	29	29
Total	15	30	45

	Value	Exact p-value
Pearson Chi-Square	40.781	<0.001

All the patients with serum estradiol value on admission greater than 79.05 expired (16 patients). Whereas all the remaining 29 patients who survived had a serum estradiol value less than 79.05

For cut off value of 79.05 of serum estradiol P value was significant i.e. <0.001.

Graph 8 : cut off value of serum estradiol relation to mortality

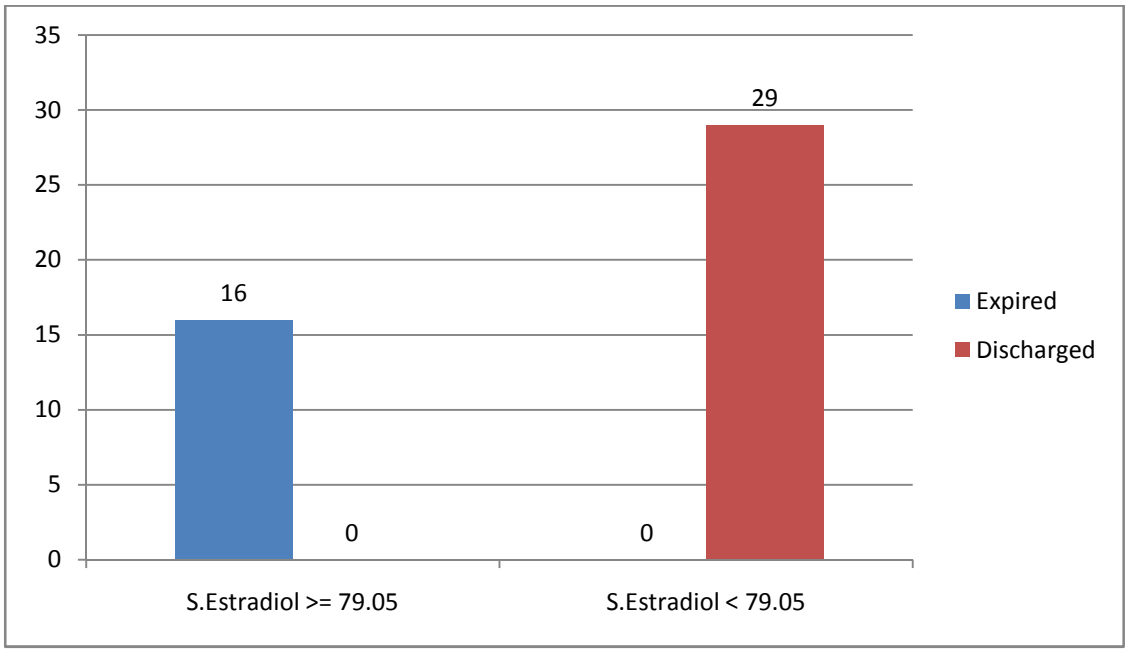
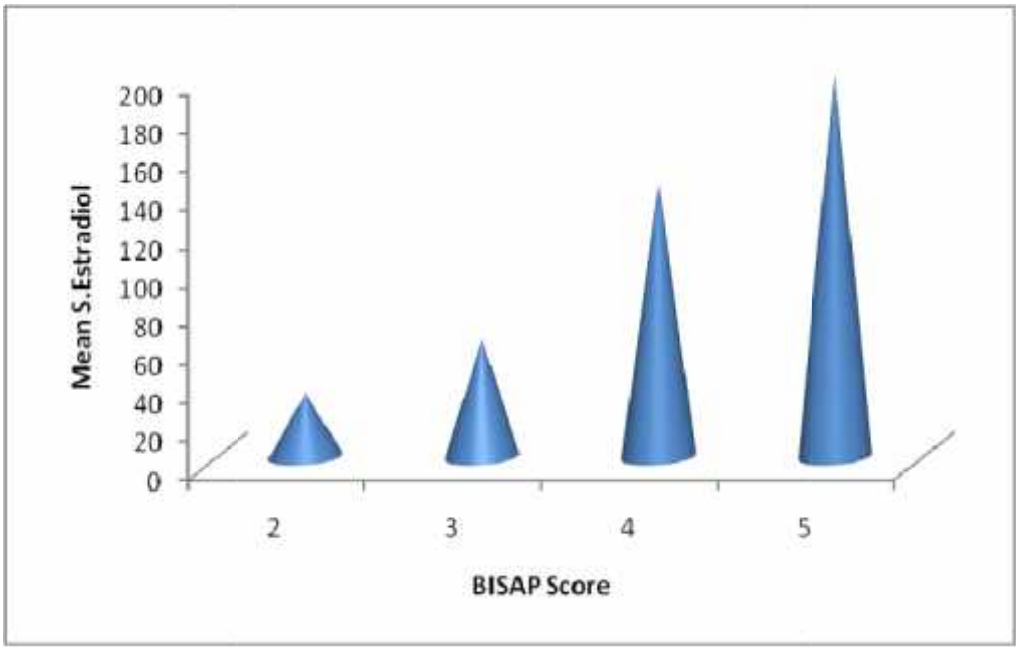


Table 10 :One way ANOVA to compare Serum estradiol in various BISAP score

BISAP Score	N	Mean value of estradiol	Minimum value of estradiol	Maximum value of estradiol
2	15	32.7607	12.21	52.90
3	14	60.9293	44.50	74.10
4	15	141.4387	84.00	376.27
5	1	198.4600	198.46	198.46
Total	45	81.4324	12.21	376.27

	Sum of Squares	Mean Square	p-value
Between Groups	109126.092	36375.364	<0.001
Within Groups	84898.916	2070.705	
Total	194025.008		

Graph 9: Comparison of serum estradiol and BISAP score



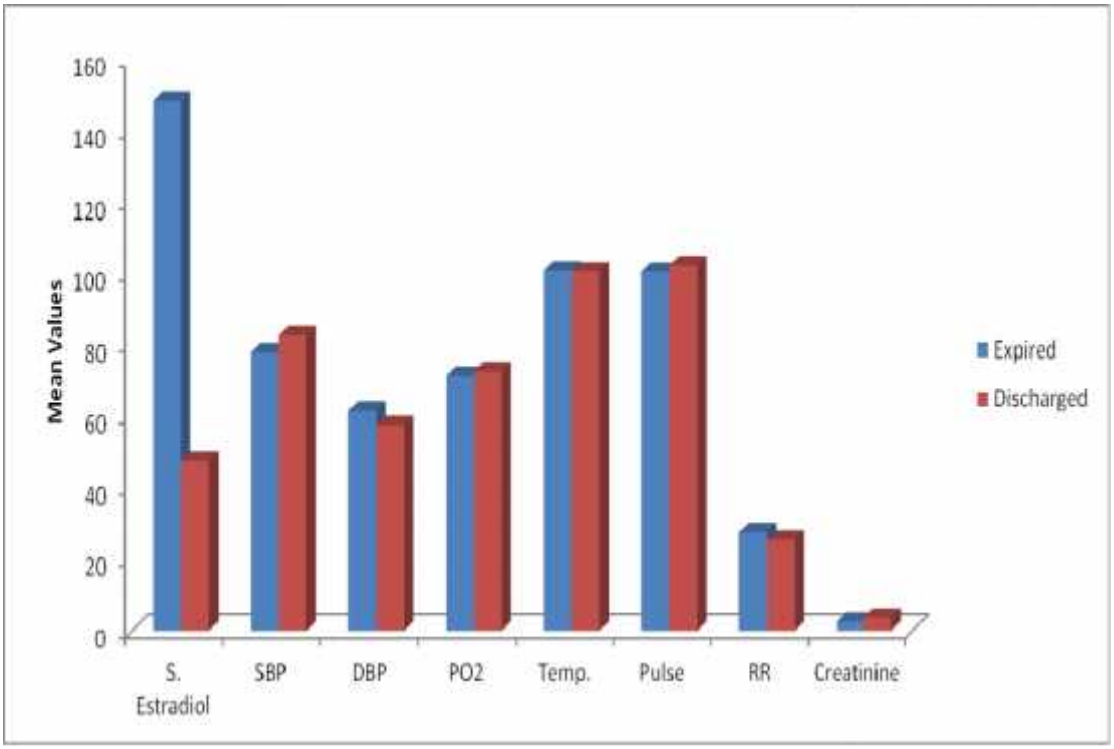
- For the category of score 2 ; there were 15 patients with mean estradiol of 32.760.
- For the category of score 3 ; there were 14 patients with mean estradiol of 60.929 .
- For the category of score 4 ; there were 15 patients with mean estradiol of 141.43. (minimum of 84 and maximum of 376).
- For the category of score 5; there was only one person with estradiol of 198.46.

After comparing BISAP score and serum Estradiol we observed a direct correlation between the two parameters with significant P value of <0.001

Table 11: Independent variables

	Outcome	N	Mean	p-value
RANSON score	Expired	15	4.8000	<0.001
	Discharged	30	3.1333	
Serum estradiol	Expired	15	148.80	<0.001
	Discharged	30	47.7473	
BISAP	Expired	15	4.0667	<0.001
	Discharged	30	2.5333	
SBP	Expired	14	78.0000	0.149
	Discharged	30	82.9333	
DBP	Expired	6	61.6667	0.145
	Discharged	21	57.7143	
PO2	Expired	15	71.6200	0.702
	Discharged	30	72.9000	
Creatinine	Expired	15	2.5253	0.623
	Discharged	30	3.5603	
Temperature	Expired	15	101.00	0.711
	Discharged	30	100.75	
Respiratory rate	Expired	15	27.6667	0.411
	Discharged	30	25.6000	
Pulse	Expired	15	100.67	0.724
	Discharged	30	102.47	

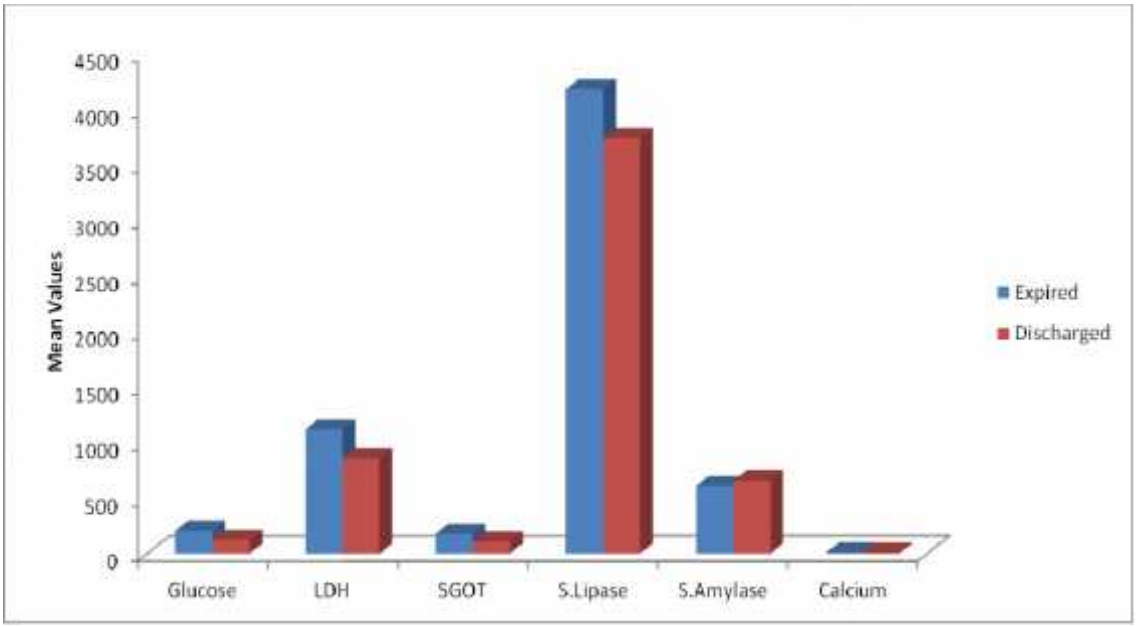
Graph 10: Independent variables



Independent Variables

	Outcome	N	Mean	p-value
WBC	Expired	15	$1.6347x10^4$	0.318
	Discharged	30	$1.4043\ x10^4$	
Glucose	Expired	15	204.67	<0.001
	Discharged	30	125.53	
LDH	Expired	15	1115.9	0.213
	Discharged	30	860.70	
SGOT (AST)	Expired	15	177.07	0.216
	Discharged	30	108.40	
Calcium	Expired	13	9.7285	0.478
	Discharged	24	8.5383	
Serum lipase	Expired	15	4179.2	0.665
	Discharged	30	3737.8	
Serum amylase	Expired	15	607.13	0.828
	Discharged	30	656.47	

Graph 11: Independent variables



DISCUSSION

There is strong evidence present in some studies suggesting that high levels of serum estradiol (E2) are associated with increased mortality in critically ill patients and in patients with severe infections [61,62] . Angstwurm et al [63] found that elevated serum estradiol correlated significantly with increased mortality in both male and elderly female patients with infection, indicating that E2 levels correlated with the prognosis of septic patients and gender of the patient did not act as a confounding factor. However, the correlation between serum E2 level and outcome in patients with SAP remained unknown.

The pathophysiology of SAP involves extensive destruction of pancreatic parenchyma, which rapidly leads to systemic inflammatory response (SIRS) and multiple organ failure. It means that SAP has a mechanism similar to that of critical illnesses such as sepsis. Although aromatase activity in SAP has not been investigated in earlier studies, there is evidence showing that aromatase activity was up-regulated following sepsis. Spartt et al. [(64)] reported that, in patients with SIRS, the expression of aromatase P 450 gene was increased, resulting in the increased aromatization of androgen and increased peripheral biosynthesis of estrogen.

Sammy et al.[65] showed that estrogen synthesis and aromatase activities of lymphocytes were increased significantly following sepsis, while the expression of estrogen receptor (ER) – BETA remained stable [65]. Their results suggested a strong association between aromatase activity and ER expression .Using the same model Schneider et al.[66] demonstrated that the administration of an aromatase inhibitor in sepsis could restore the suppressed expression of ER- BETA and the depressed immune functions of splenic lymphocytes. E2 as well as the systemic inflammatory

responses following acute illnesses are usually neither cell type specific nor insult specific.[43] It is possible that the increased E2 levels observed in SAP were due to the up-regulated aromatase activity which lead to down regulation of ER expression.

In our study elevated endogenous E2 levels were associated with poor outcome. In contrast, there are some studies which show that administration of estrogen after trauma, hemorrhage or sepsis significantly reduce mortality [67-69]. The action of estrogen relies on ER (genomic effect, slow response) or cell surface receptors such as GPR 30 (non genomic effect, rapid response) [68,69]. As the administration of E2 has been shown to rapidly restore cardio- pulmonary, hepatic and immune function following critical illness, it is likely that the action of acute pharmacological doses of estrogen is largely through the non genomic pathway. [70-72] Because conventional intracellular ERs are down regulated following critical illness the genomic effects of estrogen carried out through ER are unlikely to exert rapid response [69]. On the other hand, the role of endogenous E2 during critical illness is less clear. The above mentioned data clearly indicates that E2 administration has anti-inflammatory and immune modulating effects in many diseases. It is still not clear whether endogenous E2 is an inflammatory process mediator or whether it is simply a marker of sepsis. [62, 73, 74]

Early diagnosis of SAP is important because it might lead to a better prognosis by prompting aggressive treatments such as continuous arterial infusion of a protease inhibitor and antibiotics as well as fluids [75-77.] Some scoring systems including RANSON score, APACHE 2 score, APACHE 3 score, MODS, SOFA score and CTSI have been used to help in identifying patients with SAP who are at a risk of developing an adverse outcome [8, 78,79]. However, the utility of these scoring systems

to predict outcome in SAP patients is still inconclusive and a large amount of variation exists between different scoring systems [80-82]. Following the discovery of significant association between the effects of estrogen & ERs on organ systems during critical conditions, it will be interesting to see if estrogen levels can also be used to predict patient outcome.

To establish this relation, this cross sectional study was conducted in the department of medicine and gastroenterology of KLES Dr. Prabhakar Kore Hospital and Research Centre over a period of one year from January 2014 to December 2014. The blood samples taken from 45 patients meeting the inclusion and exclusion criteria constituted the material for study.

Total no. of cases (n) = 45 were included in our study, patients age ranged from 18 to 92 years and mean age was 38.91 years. Out of the 45 cases, 15 patients expired and 30 patients got discharged. Mean age of expired patients was 42.86 years while mean age of discharged patients was 36.93 years. Among the 45 patients, there were 41 (91.1%) males, and 04 (8.9%) females.

Out of 41 males, 13 expired and 28 got discharged with respective percentage of 31.7% and 68.3%. Out of 4 females, 2 expired and 2 got discharged with respective percentage of 50% for both.

We calculated BISAP score in all our patients. Our study showed a direct correlation between BISAP score and mortality. Out of 15 patients in score 4 category 14 patients expired and one patient improved and got discharged (93.3%). Score 5 category had only one patient with a mortality percentage of 100%; with significant p value of <0.001. While there was no mortality in score 2 and 3 categories of BISAP score.

Our results showed that the serum E2 levels in non survivors were significantly elevated at the time of ICU admission and were 3.1 times higher than those of survivors (mean-148 pg/ml Vs 47.7 pg/ml, $p < 0.001$). In addition, by applying the ROC curve model, we found that sensitivity of 100%, specificity of 96.7%, positive predictive value of 93.8% , Negative predictive value of 100% and an accuracy of 97.78% could be achieved for the prediction of mortality if a serum E2 level of 79.05 pg/ml was chosen as cut off point. These results were far better than study did by Dossett et al. [59] which showed that a serum E2 cut off value of 50pg/ml had 48% sensitivity and 80% specificity in predicting the mortality of critically ill patients.

We compared serum E2 levels with BISAP score and found that as the score went on increasing estradiol value was increased, with significant P value <0.001; suggestive of reliability of serum E2 levels as an indicator of disease severity.

Apart from this we also found direct co-relation between Glucose levels and mortality with significant p value (<0.001) suggestive of that hyperglycemia was related to poor outcome

It is well known that serum E2 levels are increased in liver cirrhosis [83], therefore we excluded patients with liver cirrhosis.

A major limitation of the present study was that no data on serial changes of E2 levels following ICU admission was collected. It is not known whether a trend of progressively increasing E2 levels during the course of SAP predicts mortality or whether a trend of E2 levels returning to the baseline indicates full recovery. A prospective cohort study done by Kauffmann et al. including 1408 critically ill patients whose E2 levels were measured on ICU admission as well as 2 to 5 days after

admission, showed that although serum E2 level measured on admission alone was a strong predictor of mortality, the power of prediction was even greater, if the trend of consecutive change in serial E2 levels was included along with admission E2 levels. Taking this observation into consideration, we feel that a similar study should be conducted in patients of SAP to verify the strength of E2 levels as a marker of prognosis.

However, to identify a patient with high risk of mortality early in the course of disease, a biomarker is less useful if it has to be measured serially to show a trend for prognosis prediction. This is because until that time the disease may have already become too advanced to start an effective treatment. From this point of view, E2 seems to be a good marker because its value can be obtained early on admission and a single value alone can be powerful enough to prognosticate SAP patients as it is in our study.

CONCLUSION

In our study, There was a positive relationship between increasing estradiol values and the increasing BISAP score in SAP patients. Serum estradiol was found to be a early and better predictor for assessing severity regardless of gender.

SUMMARY

In the present study of 45 patients titled "ESTIMATION OF SERUM ESTRADIOL LEVELS AND ITS CO-RELATION WITH BISAP (BEDSIDE INDEX FOR SEVERITY IN ACUTE PANCREATITIS) SCORE IN SEVERE ACUTE PANCREATITIS – ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY" during the period from January 2014 to December 2014 in department of Medicine and Gastroenterology of K L E S Dr. Prabhakar Kore Hospital and Research Centre, Belgaum. The findings of the study has been summarized as follows:

- Total no. of cases (n) = 45 were included in our study, patients age ranged from 18 to 92 years and mean age was 38.91 years.
- Out of the 45 cases, 15 patients expired and 30 patients got discharged. Mean age of expired patients was 42.86 years while mean age of discharged patients was 36.93 years.
- Among the 45 patients, there were 41 (91.1%) males, and 04 (8.9%) females.
- Out of 41 males, 13 expired and 28 got discharged with respective percentage of 31.7% and 68.3%. Out of 4 females, 2 expired and 2 got discharged with respective percentage of 50% for both.
- Our study showed a direct correlation between BISAP score and mortality. Out of 15 patients in score 4 category 14 patients expired and one patient improved and got discharged (93.3%). Score 5 category had only one patient with a mortality percentage of 100%; with significant p value of <0.001. While there was no mortality in score 2 and 3 categories of BISAP score

- Our results showed that the serum E2 levels in non survivors were significantly elevated at the time of ICU admission and were 3.1 times higher than those of survivors (mean-148 pg/ml Vs 47.7 pg/ml, $p < 0.001$).
- In addition, by applying the ROC curve model, we found that sensitivity of 100%, specificity of 96.7%, positive predictive value of 93.8% , Negative predictive value of 100% and an accuracy of 97.78% could be achieved for the prediction of mortality if a serum E2 level of 79.05 pg/ml was chosen as cut off point.
- We compared serum E2 levels with BISAP score and found that as the score went on increasing estradiol value was increased, with significant P value <0.001 ; suggestive of reliability of serum E2 levels as an indicator of disease severity.
- Apart from this we found that hyperglycemia was related to poor outcome with significant p value (<0.001)

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ANNEXURE – I

INFORMED CONSENT FORM

ESTIMATION OF SERUM ESTRADIOL LEVELS AND ITS CO-RELATION WITH BISAP SCORE IN SEVERE ACUTE PANCREATITIS – ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY

Objective and purpose of the study:

This research is intended to assess the utility of SERUM ESTRADIOL as an early biomarker in patients with severe acute pancreatitis. The principal investigator of the study is Dr. _____. under the guidance of Dr. _____ .

Procedure:

If you agree to be part of the research study you will be asked the history about present illness and etiologically related histroy and will be subjected to general and systemic clinical examination and investigations.

Risk and Benefits:

The only risk and possible discomfort you might get is while taking blood from my arm for the investigations. It may cause swelling, pain, redness, bruising or infection (rarely happens) at the site from where the blood is drawn.

You may not be benefited by these investigations but you will be part of this study which is going to be useful for others in future.

Alternatives

Taking part in this study is voluntary. You may choose not to take part in this study, or if you decide to take part you can later change my mind and withdraw from the study. Your decision will not change the present or future health care or other services that you receive. The study doctor or sponsorer may stop your participation in

this study any time. If you choose not to take part in the study you will receive the standard treatment for patients with your condition

Privacy and Confidentiality:

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you in this research record. Information from this study may be published but your identity will be confidential in any publication.

Institution / Sponsor's policy:

Taking part in the study will not affect the cost of treatment i.e. it will be similar to the cost of standard procedure. In the event that you become injured as a result of taking part in this study, treatment will be offered to you or you will be given information about where to receive medical care: but you/your insurance company will be responsible for the costs. However, no reimbursement, compensation or free medical care will be given.

Voluntary participation / withdrawal :

Your participation in this study is entirely voluntary and you may withdraw from the study at any time.

.**Financial incentives for participation :**

You will not be paid / offered any gifts /incentives for participating in the study.

Authorization to publish the results :

The results of the study would be forwarded to the KLE University, Belgaum as part of requirement towards the completion of MD degree, review and publishing.

Questions:

If you have any questions about your rights as a participant you may call :

Dr. Ganga Pilli,
Chairman,
JNMC Ethical committee for
Human research,
Professor and Head of dept. of
Pathology
JNMC , Belgaum.
Phone no.- 0831-2471350
Extn - 1527

CONSENT FORM

I voluntarily agree to take part in this study by signing on the line below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicated that I have read this entire consent form or it has been read to me, and has been explained to me in my vernacular language and had all my questions answered. I will be given a copy of this consent form.

Signature /Left Thumb print of the Participant or legally authorized representative.

Participant's Name/ : …….

Signature/ Left Thumb

Impression of the participant's : …….

Name of the legally

authorized representative/ Guardian : …….

Signature/ Left Thumb Impression. : …….

Witness's Name : …….

Signature/ Left Thumb Impression. :…….…..….

Investigators name and Signature : …….

Date and Place : …….

ANNEXURE – II

PROFORMA

1. SL.NO

2 NAME:

3. AGE:

4. SEX

5. OCCUPCTION:

6. RELIGION:

7. I.P. NO./O.P. NO.:

8. ADDRESS:

9. DATE OF ADMISSION:

10.DATE OF DISCHARGE:

HISTORY:

PRESENTING COMPLAINTS

HISTORY OF PRESENTING ILLNESS:

PAST HISTORY:

Significant personal history:

Significant family history

TREATMENT HISTORY:

Received any treatment for similar complaints in the past

GENERAL PHYSICAL EXAMINATION

Pallor: Yes/No

Icterus: Yes/No

Lymphadenopathy: Yes/No

Cyanosis: Yes/No

Clubbing: Yes/No

Edema: Yes/No

Vital signs:

Pulse

Blood pressure

Respiratory rate

Temperature

PaO_2

Any significant findings

SYSTEMIC EXAMINATION:

R. S.:

C.V.S.:

P.A.:

C.N.S.:

BISAP SCORE

RANSON SCORE

INVESTIGATION:

1) Serum estradiol

ANNEXURE – III

KEY TO MASTER CHART

BISAP	**:**	BED SIDE INDEX FOR SEVERITY OF ACUTE PANCREATITIS
BP	**:**	BLOOD PRESSURE
PO_2	**:**	PARTIAL PRESSURE OF OXYGEN
WBC	**:**	WHITE BLOOD CELLS
LDH	**:**	LACTATE DEHYDROGENASE
SGOT	**:**	SERUM GLUTAMIC OXALOACETIC TRANSAMINASE