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RESEARCH ARTICLE

A STUDY OF SERUM CALCIUM AND SERUM ALBUMIN LEVELS IN PREDICTING SEVERITY OF ACUTE PANCREATITIS

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Abstract

Background: Acute Pancreatitis (AP) is an acute inflammatory process of the pancreas that affects other regional tissues and more distant organ system through the systemic inflammatory response, resulting in organ dysfunction and death. Only Minority patients will develop a severe disease, while most patients suffer from a mild, self-limiting inflammatory process. About 10 to 20% of patients will progress to Severe Acute Pancreatitis (SAP) with a mortality rate of 6 to 10%. Serum calcium and serum albumin obtained within the first 24 hours of hospital admission are useful predictors of severity in Acute Pancreatitis. With an adequate interpretation of their cut-off points, they are valuable for identifying the patients that require intensive care support, even in primary and secondary care centers. So, the availability of these laboratory investigations can be used for early assessment and treatment of severe Acute Pancreatitis (SAP) and therefore helps in reducing mortality due to Acute pancreatitis. We also compared and correlated other scoring systems in predicting the severity of acute pancreatitis.

Materials and Methods: We conducted a prospective observational study of serum calcium and serum albumin levels in predicting severity of acute pancreatitis. Data was collected from 100 inpatients over 18 months admitted to in-patient in Department of general Medicine, Basaveshwara Teaching and General Hospital attached to M.R Medical College, Kalaburagi. Data was analyzed using SPSS software version 26.

Results: Total of 100 patients with 87 males and 13 females were enrolled. Among the 100 patients 31 patients developed Severe Acute Pancreatitis (SAP) marked by evidence of end organ failure, local complications like pseudocyst, and/or prolonged ICU stay of more than 7 days and 9 patients died. Among the individual parameters Serum Albumin, Serum calcium, Corrected serum calcium including TC (Total cell count), Serum Urea, Serum creatinine, Pao₂, Serum LDH showed a significant association with severity of acute pancreatitis. APACHE II systems had a sensitivity of 71.10% and

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specificity of 96.67 % in predicting severity. Sensitivity and specificity of Ranson's score was 77.42% and 96.56% respectively. BISAP score had a low sensitivity of 61.67% and high specificity 98.33% .

Conclusion: APACHE II score and Ranson's score are the best scoring systems in predicting the severity of acute pancreatitis. Parameters like Hypoalbuminemia, Hypocalcemia including Hypoxia, uremia, Acute renal failure, leukocytosis, and increase in serum LDH levels were significantly associated with Severe Acute Pancreatitis (SAP).

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Introduction:-

Acute Pancreatitis (AP) is an acute inflammatory process of the pancreas that affects other regional tissues and more distant organ system through the systemic inflammatory response (SIRS) , resulting in organ dysfunction and death⁷. Only Minority patients will develop a severe disease with local or systemic complications and / or organ failure (OF) while most patients suffer from a mild ,self limiting inflammatory process⁵. Its incidence, generally varies in the range of 20 to 40 per 100,000 population .The overall mortality rate from acute pancreatitis has substantially dropped from >10% several years ago to less than 2% in recent years¹.

The Severe Acute Pancreatitis (SAP) has been redefined as Acute Pancreatitis with persistent organ failure (Organ Failure lasts more than 48hours) with lethality rate of 20-50% according to 2012 revised Atlanta classification for Acute Pancreatitis^{2,7}.

Albumin can bind to an extremely wide range of endogenous and exogenous ligands ,to transport them to specific tissues and organs ,to increase their solubility in plasma or to dispose off when they are toxic. The chemical structure of albumin can be altered by some specific process (oxidation, glycation) leading to rapid clearance and catabolism⁷. In the progress, many disease including cancer, infection, inflammation, a low-level of serum albumin has been identified .According to the researches the phenomenon of low-level serum albumin in these diseases is due to abnormal metabolism of albumin led by inflammatory response ,as well as a low intake of albumin⁷.

Abnormal regulation of calcium signals act as pivotal trigger in pathogenesis of Acute Pancreatitis ,calcium influx is an important for maintenance of signal generation as is release of calcium from the endoplasmic reticulum³. Some authors defend that hypocalcemia can be attributed to binding of calcium in areas of fat necrosis and may also be related to altered levels of circulating parathormone in Acute Pancreatitis⁴.

Serum calcium and serum albumin obtained within the first 24 hours of hospital admission are useful predictors of severity in Acute Pancreatitis and have specificity ,sensitivity and predictive values that are comparable with other routinely used prognostic scales. With an adequate interpretation of their cut-off points, they are valuable for identifying the patients that require intensive care support, even in primary and secondary care centers⁶. So easily availability of these laboratory investigation can be used for early assessment and treatment of severe Acute Pancreatitis (SAP) and therefore helps in reducing mortality due to Acute pancreatitis⁶.

Therefore this study on serum calcium and serum albumin level in predicting the severity of Acute pancreatitis has been undertaken.

We also compared various other scoring system like RANSON'S Score, APACHE II and BISAP'S Score in predicting the severity of acute pancreatitis and correlated with the parameters.

Ranson's Score:

≥3 was taken as predictor of severe pancreatitis¹⁰.

At Admission:

1. Age in years > 55 years
2. White blood cell count > 16000 cells/mm³
3. Blood glucose > 10 mmol/L (> 200 mg/dL)

- 4. Serum AST > 250 IU/L
- 5. Serum LDH > 350 IU/L

At 48 hours:

- 1. Calcium (serum calcium < 2.0 mmol/L (< 8.0 mg/dL)
- 2. Hematocrit fall > 10%
- 3. Oxygen (hypoxemia PO2 < 60 mmHg)
- 4. BUN increased by 1.8 or more mmol/L (5 or more mg/dL) after IV fluid hydration.
- 5. Base deficit (negative base excess) > 4 mEq/L
- 6. Sequestration of fluids > 6 L

APACHE II Score > 8 suggestive of SAP

	+4	+3	+2	+1	0	+1	+2	+3	+4
1 Rectal temp (°C)	>41	39-40.9		38-38.9	36-38.4	34-35.9	32-33.9	30-31.9	<29.9
2 Mean arterial pressure (mmHg)	>160	130-159	110-129		70-109		50-69		<49
3 Heart rate (bpm)	>180	140-179	110-139		70-109		55-69	40-54	<39
4 Respiratory rate (bpm)	>50	35-49		25-34	12-24	10-11	6-9		<5
5 Oxygen delivery (mL/min)	>500	350-499	200-349		<200				
6 PO2 (mmHg)					>70	61-70		55-60	<55
7 Arterial pH	>7.7	7.6-7.69		7.5-7.59	7.3-7.49		7.25-7.3	7.15-7.2	<7.15
8 Serum sodium (mmol/L)	>180	160-179	155-159	150-154	130-149		120-129	111-119	<110
9 Serum potassium (mmol/L)	>7	6-6.9		5.5-5.9	3.5-5.4	3-3.4	2.5-2.9		<2.5
10 Serum creatinine (mg/dL)	>3.5	2-3.4	1.5-1.9		0.6-1.4		<0.6		
11 Hematocrit (%)	>60		50-59.9	46-49.9	30-45.9		20-29.9		<20
12 White cell count (103/mL)	>40		20-39.9	15-19.9	3-14.9		1-2.9		<1

	Age Points								
Age									Points
<44									0
45-54									2
55-64									3
65-74									5
>75									6
Chronic Health Points									
History of Severe Organ Insufficiency								Points	
Nonoperative patients								5	
Emergency postoperative patients								5	
Elective postoperative patients								2	

The BISAP'S Score uses five points: Urea nitrogen (BUN) >25 mg / dl, Impaired mental status by evidence of disorientation or disturbance in mental status, presence of the SIRS, Age >60 years, and Pleural effusions^{11,12}.

SIRS is defined by the presence of ≥ 2 of the following criteria¹³: pulse >90 beats / min, respirations >20 per min, or PaCO₂ < 32 mm Hg, temperature >100.4 ° F or < 96.8 ° F and white blood cell count >12,000 or < 4,000 cells per mm³ or >10 % immature neutrophils (bands)^{14,15}.

Objectives:-

1. To study Serum Calcium levels in Acute pancreatitis.
2. To study Serum Albumin levels in Acute Pancreatitis.
3. To study Serum Calcium and Serum Albumin levels in predicting the severity of Acute Pancreatitis.

Material And Methods:-

A prospective observational study was conducted on the in-patient admitted to Basaveshwar Teaching and General Hospital which is attached to Mahadevappa Rampure Medical college, kalaburagi for a period of 18 months from i.e., from 1 March 2021 to 31st August 2022.

Inclusion criteria:

1. Aged > 18 years.
2. All cases of Acute pancreatitis (irrespective of etiology)
3. The diagnosis of acute pancreatitis was based on presence of 2 of 3 following characteristic findings

Clinical criteria:

History of abdominal pain radiating to back and relieved by bending forward and associated with tenderness and guarding of upper abdomen.

Radiographic evidence:

CT/ USG findings suggestive of acute pancreatitis like pancreatic edema, pancreatic necrosis, peripancreatic fluid collection.

Biochemical:

Serum amylase and serum lipase greater than 3 times of upper limit of normal.

Exclusion criteria:

1. All those patients with chronic pancreatitis were excluded.
2. All those previously treated patients were excluded from study.
3. Other causes of Hypocalcemia.
4. Other causes of Hypoalbuminemia.

Sample size:

100 (study subjects were selected randomly based on inclusion and exclusion criteria).

Method of collection of data:

A prospective observational study was conducted on in-patients admitted in Basaveshwar Teaching and General Hospital attached to Mahadevappa Rampure Medical college, Kalburagi for a period of 18 months from 1st March 2021 to 31st August 2022 after Ethical committee approval. After obtaining informed consent, a detailed history was collected from qualifying patients using a pre-designed, structured proforma. Further, general examination and a detailed systematic examination, followed by relevant investigations were conducted and the results were noted.

Statistical Analysis:

Data was analysed by IBM SPSS 26.0 version software. Collected data were spread on excel sheet and prepared master chart. Through the master chart tables and graphs were constructed. For quantitative data analysis ANOVA, Correlation Coefficient and Un-paired t-test were applied. For qualitative data analysis chi-square test and Fisher exact probability test were applied for testing of statistical significance. If P-value was less than (<) 0.05 considered as significant.

Results:-

This study included 100 acute pancreatitis, out of which 87 were male and 13 were female. This study included 85 patients who were <55 years of age out of which 30 were severe, 55 were mild and 15 patients who were >55 years of age out of which 10 were severe, 5 were mild, thus age has no significant association in predicting severity of acute pancreatitis (Fig 2).

This study found that etiology of acute pancreatitis was Alcohol seen in 67% , Gall stones in 13% , Drug induced in 5%, Hypertriglyceridemia in 6%, Trauma in 4%, Post ERCP in 3%, Idiopathic in 2% patients (Fig 1).

Fig 1:- Pie diagram representing etiology wise distribution of acute pancreatitis patients.

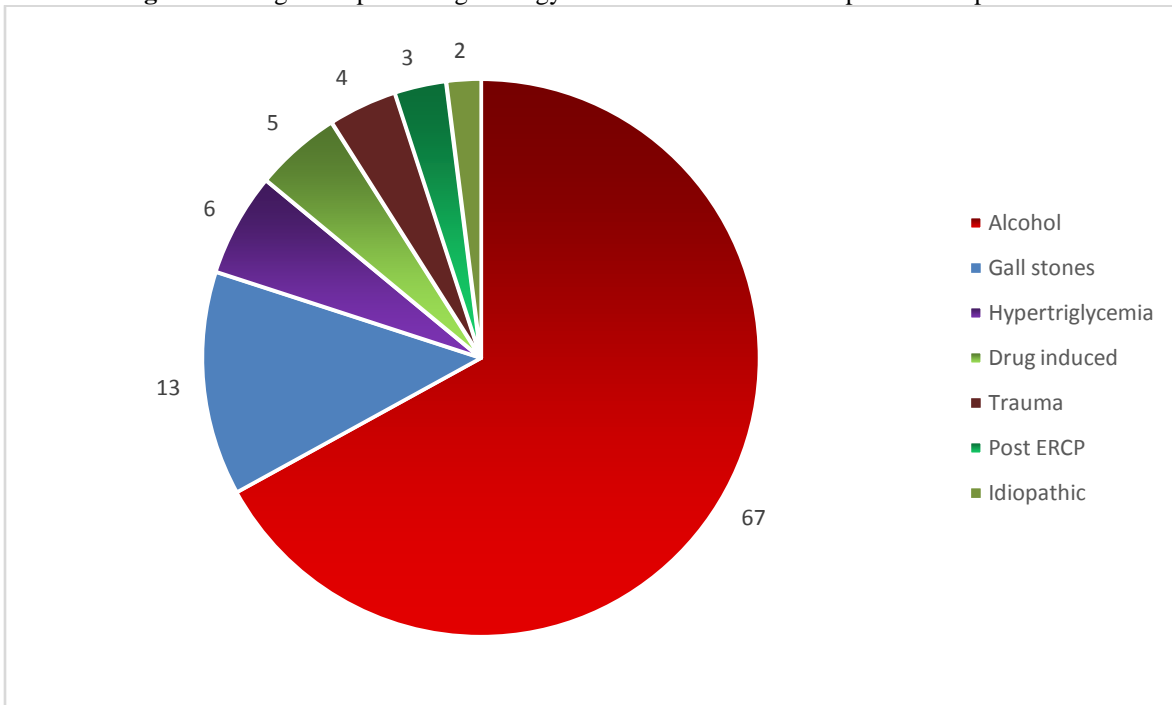
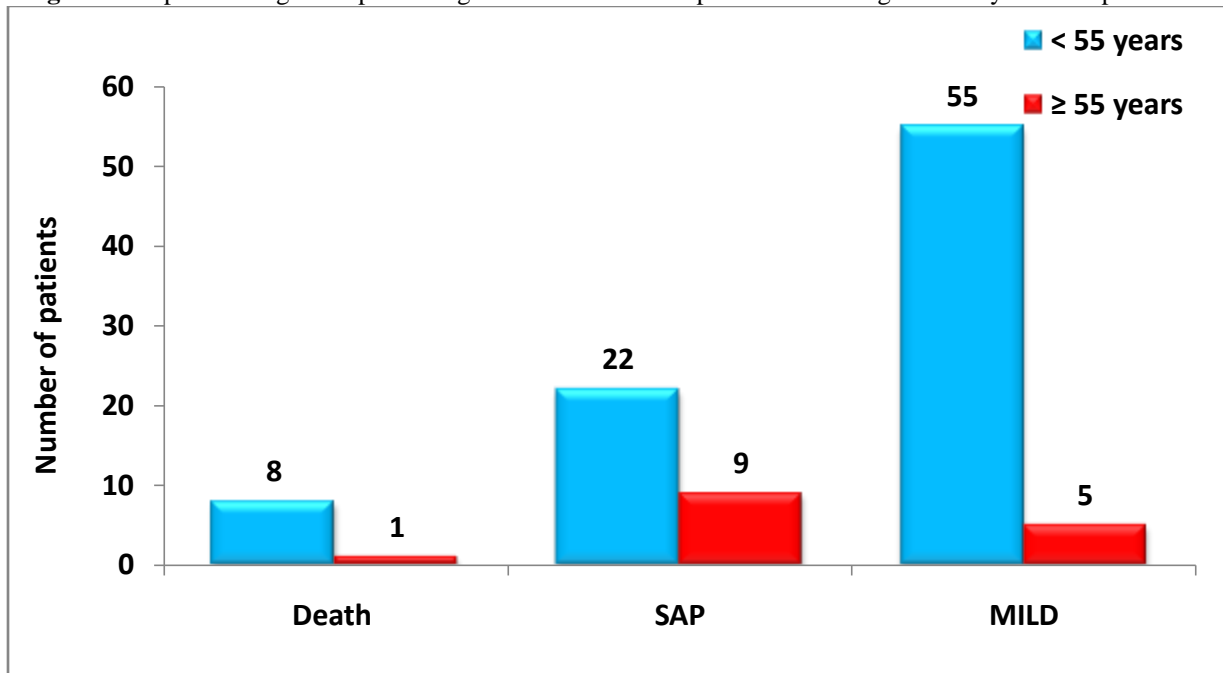
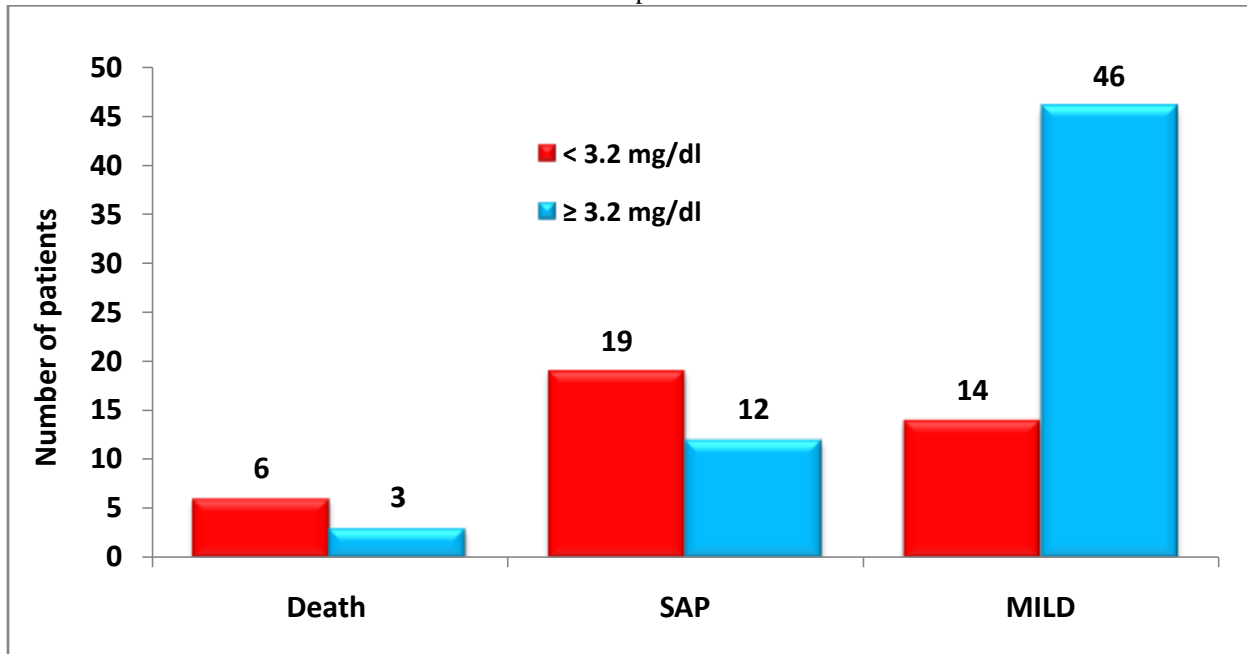


Fig 2:- Multiple bar diagram represents age wise distribution of patients according to severity of acute pancreatitis.



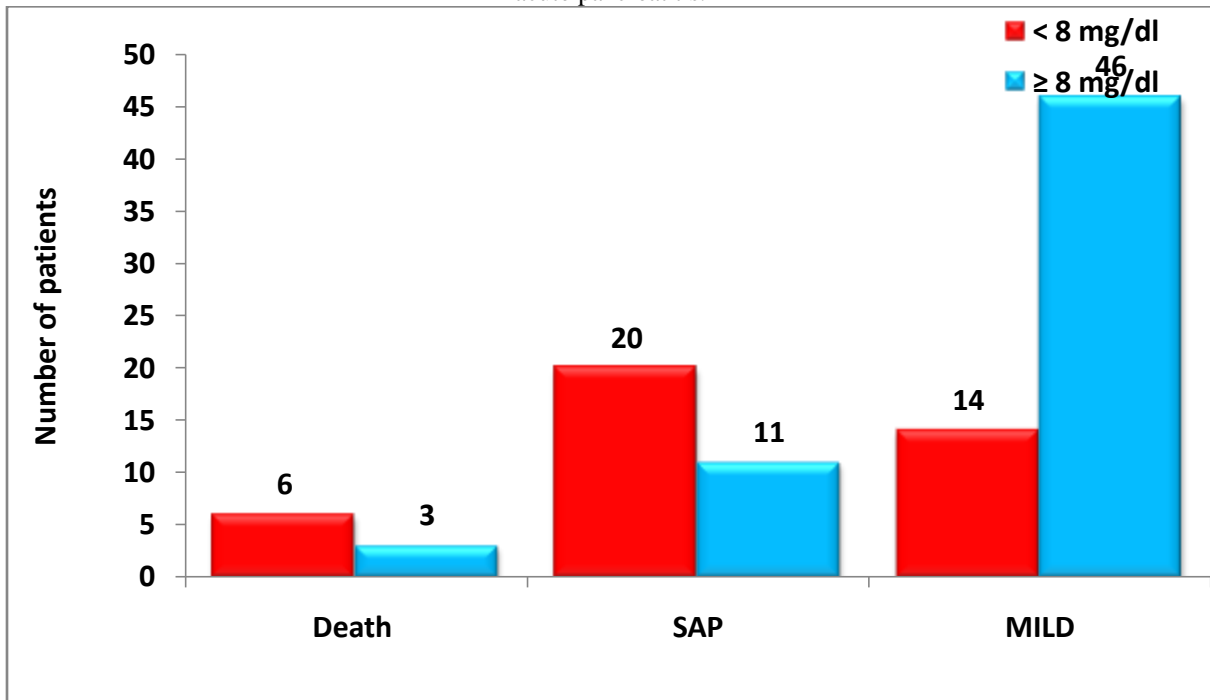
Hypoalbuminemia with cutt off Serum albumin < 3.2mg/dl was found in 33(33%) patients out of which 25 were severe (Death+SAP) and 14 were Mild and serum albumin > 3.2 mg/dl was found in 67(67%) patients of which 15 were Severe (death+SAP) , 46 were Mild, thus hypoalbuminemia has significant association in predicting severity of acute pancreatitis with p value < 0.05(Fig 3).

Fig 3:- Multiple bar diagram represents serum Albumin levels wise distribution of patients according to severity of acute pancreatitis.



Hypocalcemia with cutoff serum calcium <8 mg/dl was found in 40(40%) patients out of which 26 were severe (Death+SAP) , 14 were Mild and serum calcium > 8 mg/dl was found in 60(60%) patients of which 14 were severe (death+SAP), 46 were Mild, thus hypocalcemia has significant association in predicting severity of acute pancreatitis with p value < 0.05(Fig 6). Corrected serum calcium has also significant association in predicting severity of acute pancreatitis as albumin which act as confounding factor is also significant (Fig 4).

Fig 4:- Multiple bar diagram represents Serum calcium levels wise distribution of patients according to severity of acute pancreatitis.



TC(Total cell count) , Serum creatinine, PaO2 is found to have highly significant association with p value < 0.001 and Serum Urea, Serum LDH is found to have significant association with p value <0.05 in predicting severity of acute pancreatitis.

In our study, 35 patients had Ranson’s score ≥ 3 which included 33 patients of severe pancreatitis (including death) & 2 patients with mild pancreatitis and also found that Ranson’s Score has 100% sensitivity and 96.67% specificity in predicting Mortality(Fig 5). Sensitivity and Specificity in Predicting Severity is 77.42% and 96.57% respectively (Fig 6).

APACHE II score ≥ 8 was seen in 33 patients which included 31 patients of severe pancreatitis (including death) & 2 patients with mild pancreatitis and also found Apache Score has 100% sensitivity and 96.67% specificity in predicting Mortality(Fig 5). Sensitivity and Specificity in Predicting Severity is 71.10% and 96.67% respectively (Fig 6).

BISAP score ≥ 3 was seen in 27 patients which included 26 patients of severe pancreatitis (including death) & 1 patient with mild pancreatitis and also found BISAP Score has 77.7% sensitivity and 98.33% specificity in predicting Mortality(Fig 5) . Sensitivity and Specificity in Predicting Severity is 61.29% and 98.33% respectively (Fig 6).

Thus RANSON score and APACHE II has high sensivity with low specificity but BISAP’S Score has high specificity with low sensitivity in predicting mortality (Fig 5). Ranson Score, APACHE II has good sensitivity compared to BISAP’S Score with low specificity ,but BISAP score has high specificity in predicting severity of acute pancreatitis (Fig 6).

Fig 5:- Bar diagram represents comparison of statistics of mortality of different scores in acute pancreatitis patients.

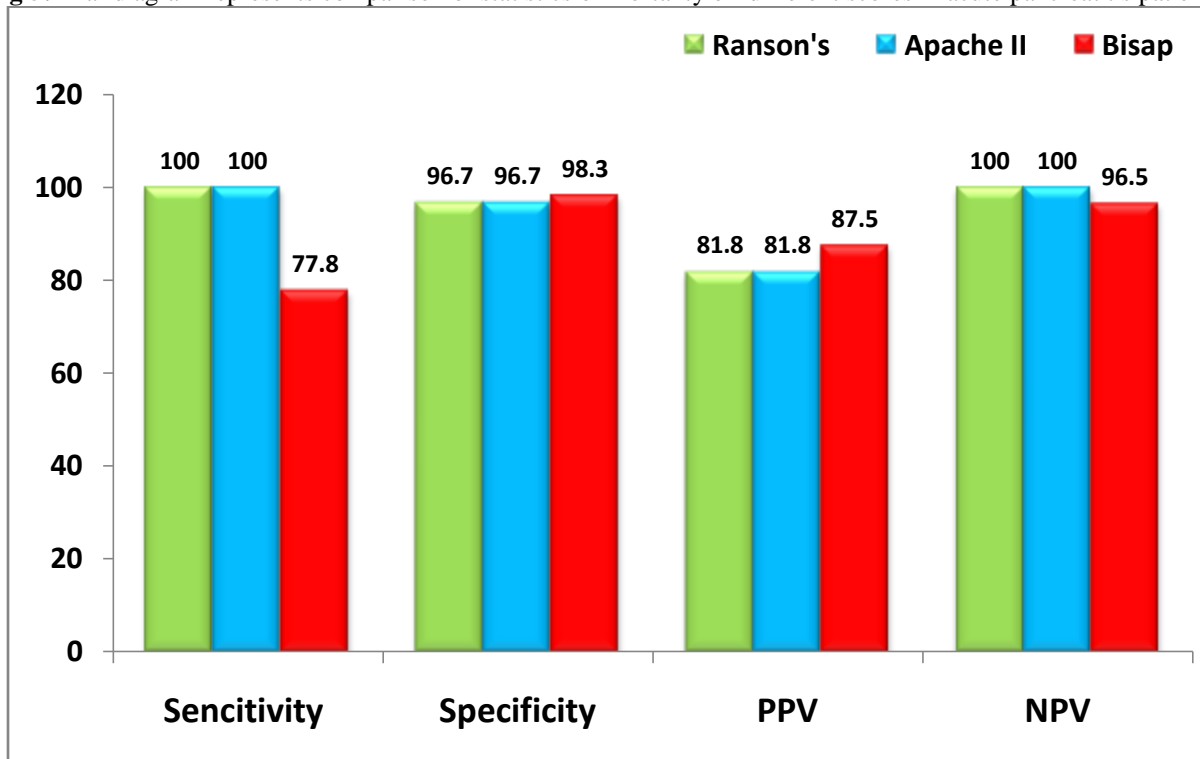
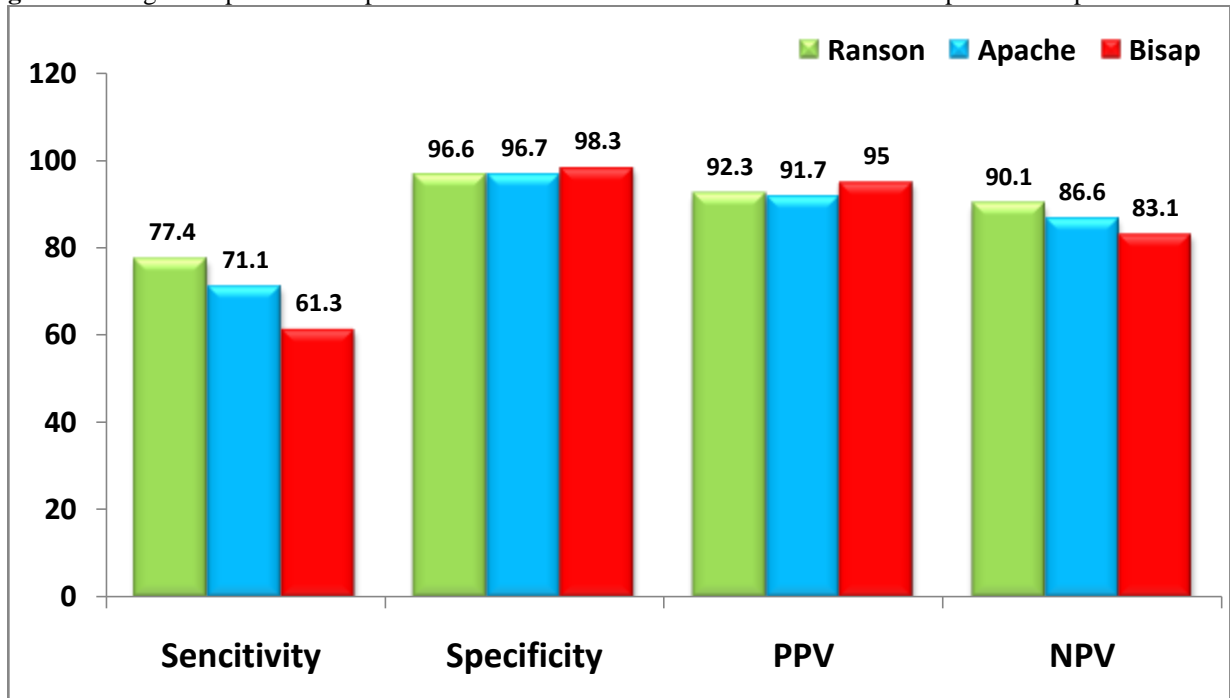


Fig 6:- Bar diagram represents comparison of statistics of different scores of severe acute pancreatitis patients.



Discussion:-

In this study we compared the accuracy of three representative prognostic multi factorial scoring systems in acute pancreatitis. We also assessed the accuracy of 12 individual parameters in assessing the severity and mortality of acute pancreatitis. 100 patients with acute pancreatitis were enrolled in our study. Among this 87 were males and 13 were females. In this 100 patients, 9 patients died i.e., the mortality rate was 11%. A total of 40 patients (including dead patients) were found to have severe acute pancreatitis (SAP).

On assessing the individual variable, we found that there was statistically significant difference exist between Severe Acute Pancreatitis and mild pancreatitis in the case of eight variables.

They include

1. Serum Albumin - 'p' value < 0.05
2. Serum calcium 'p' value < 0.05
3. Corrected serum calcium 'p' value < 0.05
4. Total cell count - 'p' value < 0.001
5. Serum. Urea - 'p' value < 0.05
6. Serum creatinine- 'p' value < 0.001
7. Pao₂ - 'p' value < 0.001
8. Serum LDH - 'p' value < 0.05

Hypoalbuminemia

In our study, serum albumin < 3.2 mg/dl was found to be a predictor of severity of Acute Pancreatitis (SAP) similar observation were made by Shoukang Li et al⁷ study which also showed that serum albumin act as predictor of persistent organ failure in acute pancreatitis.

Hypocalcemia

In our study, serum calcium < 8 mg/dl and also corrected serum calcium < 8 mg/dl both were found to be a predictor of severity of Acute Pancreatitis even though albumin acts as confounding factor in hypocalcemia. Similar findings were also observed were made by Yushan Zhang et al⁵ study showed that serum calcium on admission is independent associated with persistent organ failure in acute pancreatitis and may serve as potential

prognostic factor and other studies like Bechien.WU et al¹⁶, Cooper MJ et al¹⁸, Sournitra R Ecachempali et al¹⁶ also concluded the same.

On analyzing various scoring system, a Ranson's score ≥ 3 , Apache II > 8 and BISAP score > 3 were taken as predictor of severity of acute pancreatitis.

Apache II Score :

Among 100 patients, 33 patients had an Apache II score of >8 including all the dead patients, that means Apache II had 100% sensitivity in predicting mortality with a negative predictive value of 100. Its specificity was 96.67% of positive predictive value was 81.82%. This results corresponds to the results of Papachristou et al⁹ where they found that Apache II has a 100% sensitivity in predicting mortality.

A total of 31 patients had severe acute pancreatitis (including death patients). In this 22 patients were had SAP with Apache II > 8 , among patients with mild pancreatitis were only two had Apache II score of >8 . Thus on predicting severity Apache II had a sensitivity of 71.10%, specificity of 96.67%, PPV of 91.67% and NPV of 86.57%.

Wilson C et al¹⁹, in their study found that Apache II has a sensitivity of 82%, specificity of 74%. Study by Larvin et al⁸ also showed that Apache II has a sensitivity of 77% at the time of admission. Papachristou et al⁹ in their study also showed that Apache II has a sensitivity of 70.3% and specificity of 71.9%. Marco Simoes et al²⁰ in their study showed that APACHE II system has Sensitivity of 79.4% and specificity of 83.1% in predicting severity.

In our study, the sensitivity were similar with these studies, and the specificity in our study was more than what we found in many other studies.

RANSON'S Score :

Among 100 patients, 32 had a Ranson's score ≥ 3 , Among them 9 patients died 24 had other evidences of SAP and 2 had mild pancreatitis that means all the dead patients had a Ranson's score of ≥ 3 . ie. It has a 100% sensitivity in predicting mortality as we have seen with Apache II. The specificity was 96.67%. In predicting the severity as a whole its sensitivity was 77.42% specificity of 96.57% PPV of 92.31% and NPV of 89.23%.

In similar study, Georgios L. Papachristou et al⁹ showed that the sensitivity of Ranson's score in predicting the mortality is 100% as we have seen in our study. While the sensitivity in predicting the severity was 84.2% and specificity was 89.8% which is very much similar to our study.

In a study by Steinberg²¹ Ranson criteria have an estimated sensitivity of 72% and specificity of 76%. Marco Simoes et al²⁰ in their study showed that Ranson's system has a sensitivity of 91.2% and specificity of 71.4% in predicting severity. A meta analysis encompassing 1,300 patients reported that Ranson's has an overall sensitivity of 75% and specificity of 77%.

On comparing the different scoring systems, we found that in predicting mortality, APACHE II, RANSON'S Scoring systems had 100% sensitivity and BISAP'S Score has 77.8% while the maximum specificity was for BISAP'S Score.

But for predicting the severity RANSON'S Score performed well compared to Apache II with a sensitivity of 77.4% and specificity of 96.6%. BISAP'S Scoring system was highly specific but its sensitivity was quite low.

The APACHE II System seems to be superior to other systems because it is the only system which takes in to account of all the major risk factors that predict outcome from the disease including the acute physiological changes as well as the patient's ability to recover which may be diminished by advancing age and chronic diseases.

Our study also showed that still now RANSON'S Score remains valid for predicting the severity and mortality of acute pancreatitis. It was proved to be equally efficient when compared to the rather complex APACHE II system in predicting SAP.

BISAP'S Score

Georgios L papachirstou et al⁹ study showed that prognostic accuracy of BISAP'S score is similar to those of other scoring system but our study found that RANSON score, APACHE II has good sensitivity than BISAPS score in predicting mortality and severity of acute pancreatitis.

Conclusion:-

1. Hypocalcemia and Hypoalbuminemia can be used for initial screening within first 24 hours as they are easily available and also sensitive for predicting severity of acute pancreatitis, thus to initiate early intensive care and treatment.
2. Evidence of end organ dysfunction marked by hypoxia and acute renal failure are highly sensitive predictors of severity and mortality of acute pancreatitis.
3. Leukocytosis, uremia and increase in LDH levels are the other factors found to be significant in predicting severity of acute pancreatitis in our study.
4. RANSON'S scoring system was found to be the slightly better APACHE II to predict the outcome in acute pancreatitis in our study.
5. BISAP's scoring system even though highly specific it is less sensitive in predicting outcome in our study.
6. Future researches should focus on the incorporation of preexisting risk factors and novel accurate biomarkers in forming new scoring system.

Limitations

1. Sample size was relatively small in our study.
2. The aetiology of pancreatitis was not confounded to one as they were overlapping with others.

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