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Original Research

ROLE OF PROCALCITONIN AND MONOCYTE DISTRIBUTION WIDTH LEVELS AS PREDICTOR OF SEVERITY OF ACUTE PANCREATITIS

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ABSTRACT

Introduction- Acute pancreatitis is a mild self-limiting to severe life-threatening disease. Various scores and biomarkers predicting the outcome and severity of acute pancreatitis are available. **Aim of study** – To determine the role of biochemical markers like Procalcitonin (PCT) and Monocyte distribution width (MDW) in predicting severity of acute pancreatitis. **Materials and methods** – This prospective study was conducted on patients with Acute pancreatitis (Mild and Moderate-severe) admitted in the department of General surgery at DMCH, Ludhiana. Sample size was calculated as 120 patients. Clinical and laboratory data including values of PCT, MDW, CRP, serum amylase along with other parameters were recorded. Combined values of PCT and MDW were statistically analysed. **Results**- Out of 120 patients, 65 (54.2 %) patients had mild and 55(45.8%) had moderate-severe pancreatitis. Male predominance (74.2%) was seen with most common aetiologies being alcohol and gall stone. It was observed that combined values of PCT and MDW have better sensitivity than individual markers and better role in severity assessment. PCT and MDW combined have sensitivity of 70.91%, specificity of 55.38%, PPV of 57.35%, NPV of 69.23%. and accuracy of 62.50%. **Conclusion**- Early diagnosis plays an important role in its management. Inflammatory markers like PCT & MDW are easily available and can help in early prediction of severity and reduce the complications.

Keywords – Acute pancreatitis (AP), Procalcitonin (PCT), Monocyte distribution width (MDW)

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INTRODUCTION

Acute pancreatitis (AP) is a common gastrointestinal disease with a rising incidence worldwide. It is an inflammatory disease of the exocrine pancreas which ranges in severity from mild self-limiting to severe life threatening disease. To assess the outcomes and disease severity, multiple clinico-biochemical scores, radiological imaging, and biochemical markers are used. AP is defined according to the Revised Atlanta Criteria by presence of at least 2 of the Characteristic epigastric pain, Amylase/lipase > 3x upper normal limit or characteristic imaging findings. [(1)]

Patients usually present as acute onset of severe epigastric pain radiating to the back often necessitating urgent hospital admission. [(2)] It is usually associated with episodes of vomiting. Most

patients present within the initial 24 hours of onset of symptoms. AP is categorized as mild, moderate or severe. In mild disease there is no organ failure or local complications, moderate disease is characterized by local complications or transient i.e. less than 48 hours of organ dysfunction and severe disease with persistent (>48 hours) of organ dysfunction. Organ dysfunction is classified according to Modified Marshalls scoring system with a score of more than 2 as organ failure.[3]Various etiologies have been identified with the most common being cholelithiasis, alcohol intake, hypertriglyceridemia, hypercalcemia, trauma or drugs induced. The outcome primarily depends on the severity of the disease. Early diagnosis and timely treatment is life saving. Therefore, two such markers for early identification are Procalcitonin (PCT) and Monocyte Distribution Width (MDW) included in this study.[3,4] PCT is an acute phase reactant, blood levels rises within 3-6 hours and continues till inflammatory process stays. Due to its short half-life (approx. 24hours), it is emerging as an ideal biomarker to diagnose early sepsis and inflammatory condition. [5] Monocyte distribution width (MDW) is a newer haematological parameter that measures the variability in the size of monocytes that reflects changes in immune response and the extent of inflammation, making MDW a potentially valuable parameter in the assessment of disease severity.[6]

Current markers, while useful, may have limitations in sensitivity and specificity. Most of the studies have showed individual role of markers on disease severity. By investigating the combined roles of PCT and MDW, this study aims to enhance accuracy for the severity of acute pancreatitis, potentially leading to clinical decision-making and patient outcome.

MATERIALS AND METHODS

SOURCE OF DATA

This Prospective study was done on patients diagnosed with acute pancreatitis in the department of General Surgery and Allied specialties at Dayanand medical college and hospital, Ludhiana.

METHOD OF COLLECTION OF DATA

All patients detected with AP were included in the study. Consent was obtained and relevant detailed history elicited. Findings of general physical and systemic examination were recorded.

Inclusion criteria- All patients age >18 years diagnosed with AP with typical abdominal pain, serum lipase or amylase > 3 times the upper limit of normal and characteristic CT findings were included. Patients with pancreatic cancer, previous drainage or surgery for necrosis or not willing to take part in the study were excluded.

Patients were grouped into mild, moderate and severe pancreatitis according to **Revised Atlanta criteria-**

- **Mild attacks** – minimal organ dysfunction and recovery without problems.
- **Moderately severe** – organ failure that resolves within 48 hours or local and systemic complications without persistent organ failure
- **Severe attacks** – persistent organ failure (> 48 hours)

Investigations including Hemogram with MDW(Monocyte Distribution Width), SGOT(Serum Glutamic Oxaloacetic Transaminase) , SGPT(Serum Glutamic Pyruvic Transaminase), CRP(C-reactive protein), PCT(Procalcitonin), AMYLASE, LIPASE,SERUM CREATININE,ABG(Arterial Blood Gas) were done.

General status, severity, outcomes and complications were compared with MDW, PCT and various clinical parameters to establish relationship between the same.

Sample size Calculation

It is assumed that the prevalence rate for acute pancreatitis is 7.9 per100000 (International journal of advanced medicine. June 2021) Assumptions:

Confidence level = 95% Precision (d) = +- 5%

For estimation of sample size, the following formula has been used n = (Z2 a x p x (1-p)/d2 where Za= value of standard normal variate corresponding to a level of significance

P = likely value of parameter Q = 1-P

D = margin of errors which is a measure of precision

With these assumptions the sample size works out to be around 120.

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STATISTICAL ANALYSIS

Data were described in terms of range; mean ±standard deviation (±SD), frequencies (number of cases) and relative frequencies (percentages) as appropriate. Comparison of quantitative variables between the study groups was done using Mann Whitney U test .For comparing categorical data, Chi square ($\chi 2$) test was performed and fisher exact test was used when the expected frequency is less than 5. Receiver operator characteristics (ROC) curve was done, and criterion value was estimated depending on the specificity and sensitivity. Area under curve (AUC) was measured. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations were done using (Statistical Package for the Social Science) SPSS 21.0 version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

RESULTS

A total of 120 patients with acute pancreatitis were studied out of which 65 (54.2 %) patients had MAP and 55(45.8%) patients were studied as M+SAP. Male predominance (74.2%)was seen with mean age of 41.75 years for MAP and 45 years for M+SAP (Fig.1) The most common aetiologies were alcohol and gall stone. (Table.1). While abdominal pain was the single most consistent presenting complaint. Other symptoms like vomiting, fever, and SOB were more common in M+SAP. Maximum patients (50.8%) presented within 2 days after the onset of symptoms (Fig-2). Several laboratory parameters including PCT, MDW and CRP were done which showed statistically significant differences between MAP and M+SAP, indicating potential markers for severity assessment. PCT and MDW combined could predict disease severity with sensitivity of 70.91%, specificity of 55.38%, PPV of 57.35%, NPV of 69.23%. and accuracy of 62.50%.(Table.3) Complications including Acute kidney injury, pleural effusions, respiratory distress were predominantly seen in M+SAP (Table-2). Out of the total patients, 98 were discharged under satisfactory conditions (Table-2).

Figure1 .Age wise distribution of patients.

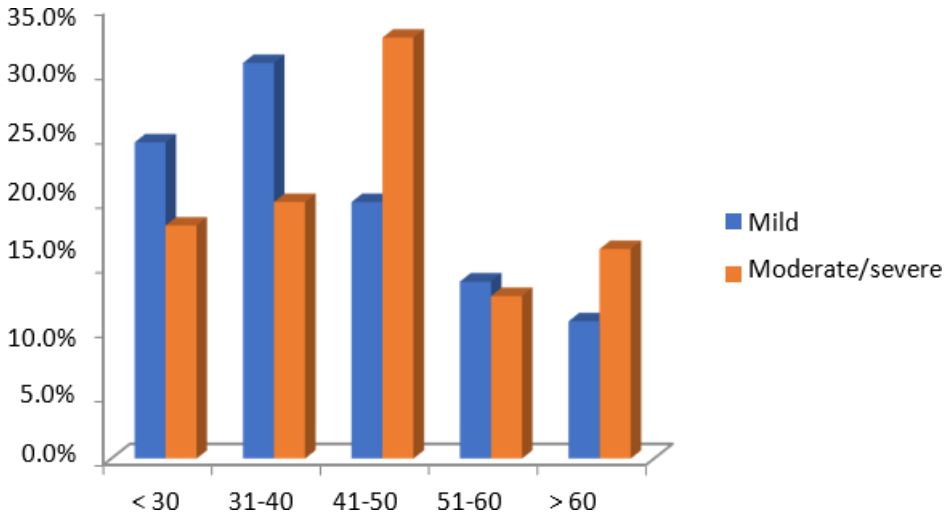

Figure 2: Duration in days since onset of symptoms

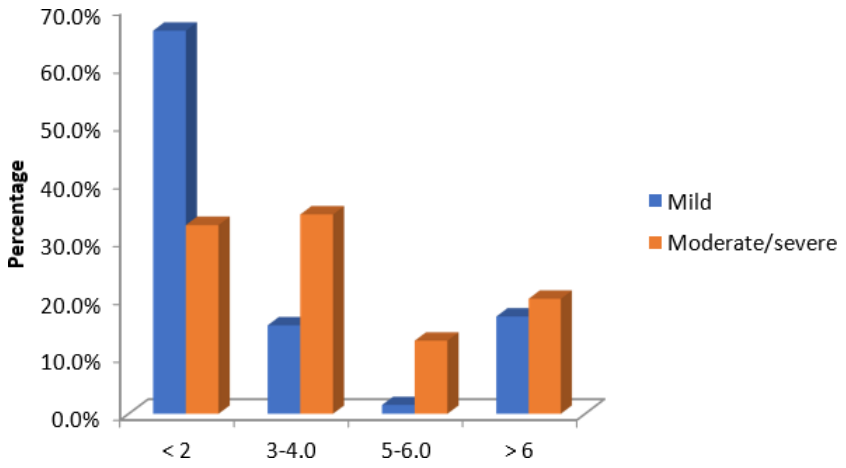

TABLE 1- Distribution based on etiology

ETIOLOGY	Mild (n=65)		Moderate/severe (n=55)		Total	
	No. of cases	%age	No. of cases	%age	No. of cases	%age
GALL STONE INDUCED	25	38.50%	25	45.50%	50	41.70%
TRIGLYCERIDES	3	4.60%	1	1.80%	4	3.30%
ALCOHOLIC	27	41.50%	27	49.10%	54	45.00%
TRAUMATIC	2	3.10%	3	5.50%	5	4.20%
HYPERCALCEMIA	0	0.00%	1	1.80%	1	0.80%
DRUG INDUCED	2	3.10%	1	1.80%	3	2.50%
IDIOPATHIC	4	6.20%	2	3.60%	6	5.00%

TABLE 2- Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of PCT, MDW and combined PCT and MDW in predicting severity of disease

Statistic	Sensitivity	Specificity	PPV	NPV	Accuracy
PCT	70.91%	55.38%	57.35%	69.23%	62.50%
MDW	27.27%	96.92%	88.24%	61.17%	65.00%
PCT+MDW	70.91%	55.38%	57.35%	69.23%	62.50%

DISCUSSION

In our study of 120 patients, 65 were MAP and 55 were M+SAP according to the Revised Atlanta criteria. Majority of the cases were mild. In contrast, Wang et al reported , 30 patients (29.13%) with MAP and 73(70.19%) with M+SAP. [7] Frequency of both MAP and M+SAP was found to be higher in males with 73.8% in MAP and 74.5% in M+SAP. Similar gender predilection was reported in studies by Mukherjee et al and Wang et al. In contrast, in some studies female predominance (60%) was reported.[8,9] Also, Nesvaderani et al. in their retrospective study on AP, reported 50.4% females and 49.6% males. [10]

Majority of patients with MAP were in age group 31-40 years whereas, M+SAP were in 41-50 years. Our study showed younger age predominance in comparison to other studies. [7] In contrast to our study, mean age of 57 and 58 years for MAP and M+SAP respectively was reported. [9]

In our study more than 50% of patients presented within 48 hours of symptom onset and around 18% presented after 6 days. The patients who presented earlier, were those with MAP (66.2%) as compared to with M+SAP (32.7%). This difference could be attributed as ours being a tertiary care center, some of these patients were referred or took discharge from other hospitals. Some of them didn't get a consultation done until the symptoms worsened. Diverse etiologies of acute pancreatitis were seen, with alcohol induced (45%) and gall stone induced pancreatitis (41.7%) being the most common. Other less common causes included 4.2% cases secondary to trauma, 3.3% attributable to hypertriglyceridemia, 0.8% to hypercalcemia, 2.5 %drug induced and 5 % cases were found to be idiopathic. Similarly, Surana P et al reported alcohol intake the most common etiology in both groups, being 41.17% in MAP and 54.83% in M+SAP followed by miscellaneous and idiopathic. [11] In contrast to our study, the most frequent etiology observed was gallstones (56%) followed by idiopathic (26%), AP secondary to ERCP (12%) and hypertriglyceridemia (6%) patients. [12] Some other retrospective studies showed a 1:1 ratio of alcohol and gallstone pancreatitis. [13]

TABLE 3- Characteristics of the study subjects.

	Mild		Moderate/severe		Total	
	No. of cases	%age	No. of cases	%age	No. of cases	%age
SEX						
FEMALE	17	26.20%	14	25.50%	31	25.80%
MALE	48	73.80%	41	74.50%	89	74.20%
PRESENTING COMPLAINTS						
PAIN ABDOMEN	65	100.00%	55	100.00%	120	100.00%
VOMITING	20	30.80%	32	58.20%	52	43.30%
NAUSEA	16	24.60%	13	23.60%	29	24.20%
SIGNS						
TENDERNESS	57	87.70%	48	87.30%	105	87.50%
PLEURAL EFFUSION	0	0.00%	25	45.50%	25	20.80%
PALLOR	2	3.10%	0	0.00%	2	1.70%
COMPLICATIONS						
AKI	0	0.00%	21	38.20%	221	17.50%
RESPIRATOTY FAILURE	0	0.00%	6	10.90%	6	5.00%
PLEURAL EFFUSION	0	0.00%	13	23.60%	113	10.80%
SHOCK	0	0.00%	5	9.10%	5	4.20%
OUTCOME						
DAMA	1	1.50%	10	18.20%	11	9.20%
DISCHARGE ON REQUEST	0	0.00%	8	14.50%	8	6.70%
DISCHARGED	64	98.50%	34	61.80%	98	81.70%
EXPIRED	0	0.00%	3	5.50%	3	2.50%

Like most of the other studies, 100% of patients in our study had a common presenting complaint of pain abdomen followed by vomiting (43.3%) and nausea (24.2 %). Similar trends were reported in other studies. [7,9] These findings indicate that while abdominal pain was a universal complaint, other symptoms like vomiting was more common in M+SAP cases, suggesting a potential correlation between the symptoms and the severity of the condition.

The study examined tenderness as the most common sign, observed in 105 patients (87.5%), with similar rates in both mild (87.7%) and M+SAP cases (87.3%). Pleural effusion was present in 25 cases (20.8%), exclusively in the M+SAP group (45.5%). Pallor was seen in 2 mild cases (1.7%), while Icterus affected 8 patients (6.7%), mainly in M+SAP cases (12.7%). These findings indicate association of pleural effusion and ascites with increased severity in patients with similar clinical presentations.

Among systemic complications, acute kidney injury (38.2%) was the most encountered followed by pleural effusion and shortness of breath (23.6%); and shock in 9.2 % patients with M+SAP. Similarly in study by Qi Yang He et al reported acute renal failure in 16% and respiratory complications in 8% of patients. [14] Albulushi et al. found that 64% of the severe cases experienced complications compared to 25% in mild cases. This sequence is logical in the term that patients with severe acute pancreatitis had more morbidities compared to mild and moderate cases. [15]

Sensitivity and specificity of procalcitonin in predicting M+SAP in our study were 70.9 % and 55.4 % respectively in comparison to 78.20 % and 69.10% as found by QiYong He et al. [14] In a study by Cai et al. it was observed that serum PCT is valuable to monitor clinical response and have a role in deescalating antibiotic therapy in AP. [16]

In our study, sensitivity of 32.7 % and specificity of 87.7% seen for MDW. Similar results were seen in a study by Abdullah Senlikci et al. [9] This contrasted with the study by Crouser ED et al. which showed sensitivity of 77% and specificity of 73%. [17] The positive and negative predictive values of PCT in our study in predicting disease severity were 57.35% and 69.23% respectively and that of MDW were 88.24% and 61.17% respectively. However, combined values of PCT and MDW were found to have a sensitivity of 70.91% and specificity of 55.38% in predicting disease severity with PPV of 57.35% and NPV of 69.23%.

Among the 120 patients, 98.5% with Mild acute pancreatitis were discharged in satisfactory condition. Among patients with Moderate-severe pancreatitis 61.8% were discharged in stable condition, 14.5% were discharged on request, 18.2% took discharge against medical advice and 5.5% expired. As

comparable to our study,16% mortality was reported in other studies (7). In contrast, there was no death among the 174 patients secondary to acute pancreatitis in a study (15). Whereas 1% mortality was seen in other study. (10). Similarly another recent study has also observed low mortality rates of 0.08% which attributed to earlier recognition of severe pancreatitis and the immediate hospital care.(18,19) Hence various lab parameters including inflammatory markers, volumetric cell indices, leucocyte counts, levels of pancreatic enzymes and serum creatinine values can be predictive of severe disease at the time of initial presentation and allow early intensive measures to be taken. Our study shows significant role of procalcitonin and MDW levels in early prediction of severity of disease and procalcitonin levels in prediction of organ failure.

CONCLUSION

Acute pancreatitis is a commonly encountered disease in surgical hospitalization. Accurate assessment of the severity is of paramount importance for its treatment and prognosis. However, the usually used scoring systems and scores in clinical practice are complicated and not precise enough leading to the failure of their clinical application. No one tool works well for all forms of acute pancreatitis. Also, some of them include assessment of parameters at 48-72 hours of admission. Hence, PCT and MDW are novel markers which show potential in various studies to serve this purpose.

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