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Comparative evaluation of Mean Platelet Volume, Serum C-reactive protein, RANSON's Score and BISAP Score in prediction of severity in acute pancreatitis patients

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Abstract
Introduction: *Acute pancreatitis (AP) is an acute inflammatory disease that can have various clinical courses. While majority of the cases heal without sequels, 10-20% of these can have severe course, and out of them 30% can be fatal. Early prediction of severity is clinically important since outcome of mild acute pancreatitis (MAP) is better than that of severe acute pancreatitis (SAP).*
Several prognostic scoring systems and inflammatory markers have been studied with the purpose of determining the severity of acute pancreatitis. In this context the most frequently used scoring systems and inflammatory markers included RANSON's Score, BISAP Score, S.C-Reactive Protein (S.CRP) and Mean Platelet Volume (MPV).
Aims and Objectives: *Comparative evaluation of MPV, S.CRP, RANSON'S Score and BISAP Score in prediction of severity of acute pancreatitis.*
Methods: *This prospective observational study was done during the period of June 2017 to November 2018 in JLN Medical College and Associated Hospital, Ajmer. The study included 100 patients of acute pancreatitis irrespective of age, sex, ethnicity or etiology.*
Result: *all 4 markers (MPV, S.CRP, RANSON's score and BISAP's score) were highly significant to predict severity of acute pancreatitis. BISAP's score was best to predict severity (at cut off value of 4) in comparison to other 3 markers. S.CRP and RANSON's score were equally sensitive to predict severity but better than MPV. MPV and S.CRP were nearly equally specific to predict severity but their specificity were higher than that of RANSON's score. Positive Predictive Value of MPV was very high in comparison to S. CRP and RANSON's score to predict severity. Negative Predictive Value of S. CRP and RANSON's score were nearly equal to predict severity, and both have better Negative Predictive Value then MPV.*
Conclusion: *MPV, S.CRP, RANSON's score and BISAP score, all four markers can be used to predict the severity of acute pancreatitis. BISAP score was found to be the best predictor of severity of acute pancreatitis among all four markers. BISAP score equal to or greater than 4 invariably indicates severe acute pancreatitis. Prognostic accuracy of RANSON's score and S.CRP is better than MPV in terms of sensitivity but less sensitive and specific than BISAP. MPV is also a good prognostic marker in terms of its specificity and easy availability in prediction of severity of acute pancreatitis.*
Keywords: *acute pancreatitis, severity, MPV, S.CRP, RANSON's score and BISAP's score.*

Introduction

Acute pancreatitis (AP) is an acute inflammatory disease that can have various clinical courses. While majority of the cases heal without sequels, 10-20% of these can have severe course, and out of them 30% can be fatal. Early prediction of severity is clinically important since outcome of mild acute pancreatitis (MAP) is better than that of severe acute pancreatitis (SAP).

Several prognostic scoring systems and inflammatory markers have been studied with the purpose of determining the severity of acute pancreatitis. In this context the most frequently used scoring systems and inflammatory markers included RANSON's Score, BISAP Score, S.C-Reactive Protein (S.CRP) and Mean Platelet Volume (MPV).

RANSON's score have been most widely used for assessment of the severity. This score is calculated on admission and 48 hrs after presentation, predicts severity and thereby need to admit in ICU**.** BISAP is simple to calculate, requires only physical examination ,vital signs, laboratory data and imaging for detection of pleural effusion that are commonly documented within 24hrs of presentation**.** S.CRP estimation is cheap and readily available. CRP is not used in the diagnosis of acute pancreatitis but as an adjunct to predict severity. Vascular thrombosis and systemic hypercoagulable states are known complications of pancreatitis. Higher levels of mean platelet volume (MPV) have been associated with thrombotic diseases. AP constitutes a systemic inflammatory process which is often accompanied by thrombosis and bleeding disorders. MPV is an index of platelet activation and reported to be influenced by inflammation.

So in this study we aimed to compare MPV, S.CRP, RANSON'S Score and BISAP Score in prediction of severity of acute pancreatitis.

Aims and Objectives

Comparative evaluation of MPV, S. CRP, RANSON'S Score and BISAP Score in prediction of severity of acute pancreatitis.

Methods

This prospective observational study was done during the period of June 2017 to November 2018 in JLN Medical College and Associated Hospital, Ajmer. The study included 100 patients of acute pancreatitis irrespective of age, sex, ethnicity or etiology.

Inclusion Criteria: Patients of acute pancreatitis diagnosed on clinical, biochemical and imaging ground irrespective of age, sex, ethnicity or etiology.

Exclusion Criteria: Patients with hematologic diseases, chronic liver disease, advanced cardiac diseases, chronic kidney disease and patients on drugs affecting platelet functions were excluded from the study.

After taking relevant history and written consent from the patient, these patients were subjected to complete clinical examination, routine investigations, radiological imaging and special investigations like MPV and Serum CRP. All data were recorded as per the enclosed proforma.

The data was coded and entered into Microsoft Excel spreadsheet. Analysis was done using SPSS version 20 (IBM SPSS Statistics Inc., Chicago, Illinois, USA) Windows software program. Descriptive statistics included computation of percentages, means and standard deviations. The independent t test (for quantitative data within two groups) was used for quantitative data comparison of all clinical indicators. Chi-square test used for qualitative data whenever two or more than two groups were used to compare. Level of significance was set at $P \leq 0.05$.

Results

Table 1

Parameters	Mild Pancreatitis group (Mean+ S.D.)	Severe Pancreatitis group (Mean+ S.D.)	P value
Mean Age(years)	40.43 ± 12.08	48.0 ± 11.41	0.02
Sex(male/female)	94% /6%	88.2% / 11.8%	0.39
Etiology (Alcohol/Gallstone)	89.2% / 10.8%	100% / 0%	0.15
Mean Glucose(mg/dl)	262.43 ± 55.94	293.05 ± 48.97	0.03
Mean Total bilirubin(mg/dl)	1.77 ± 0.63	1.45 ± 0.66	0.06
Mean AST(U/L)	173.86 ± 104.38	226.88 ± 94.12	<0.01
Mean ALT(U/L)	312.21 ± 159.15	297.58 ± 198.27	0.59
Mean LDH(U/L)	248.45 ± 116.26	381.52 ± 39.96	<0.001
Mean Amylase(U/L)	2757.4 ± 1736.77	3007.23 ± 1552.56	0.58
Mean Lipase(U/L)	1679.03 ± 936.808	1726.47 ± 1049.99	0.85
Mean MPV(fl)	8.02 ± 1.33	11.29 ± 1.26	0.001
Mean CRP(mg/dl)	3.909 ± 2.24	10.73± 4.18	<0.001
Mean RANSON's score	1.98 ± 0.74	3.705 ± 0.77	<0.001
Mean BISAP score	1.86 ± 0.53	4.23 ± 0.43	0.001

Out of 100 patients in our study, 83 were of mild pancreatitis and 17 were of severe pancreatitis. Mean age of severe pancreatitis group (48.0 ± 11.41years) was significantly higher as compared to mild pancreatitis group (40.43 ± 12.08years). Male gender was predominant in both mild pancreatitis group (94.0%) and severe pancreatitis group (88.2%) in comparison of female gender (6.0 %and 11.8% respectively). Alcohol was the main etiology in both mild pancreatitis group (89.2%) and severe pancreatitis group (100.0%) followed by gall stone.

Mean glucose level in severe pancreatitis group was significantly higher as compared to mild pancreatitis group (293.05 ±48.97 mg/dl v/s 262.43 ± 55.94 mg/dl). Mean total bilirubin in mild pancreatitis group was higher as compared to severe pancreatitis group (1.77 ± 0.63 mg/dl v/s1.45 ± 0.66 mg/dl). Mean AST in severe pancreatitis group was significantly higher as compared to mild pancreatitis group (226.88 ± 94.12 U/L v/s 173.86 ± 104.38 U/L). Mean ALT in severe pancreatitis group (297.58 ± 198.27 U/L) was lower as compared to mild pancreatitis group (312.21 ± 159.15 U/L). Mean LDH in severe pancreatitis group was highly significant compared to mild pancreatitis group (381.52 ± 39.96 U/L v/s 248.45 ± 116.26 U/L).

Mean Amylase level in severe pancreatitis group (3007.23 ± 1552.56 U/L) was higher as compared to mild pancreatitis group (2757.4 ± 1736.77 U/L). Mean lipase level in severe pancreatitis group (1726.47 ± 1049.99 U/L) was higher as compared to mild pancreatitis group (1679.03 ± 936.808 U/L).

Mean MPV level in severe pancreatitis group was highly significant compared to mild pancreatitis group (11.29 ± 1.26 fl v/s 8.02 ± 1.33 fl).Mean CRP level in severe pancreatitis group was also highly significant compared to mild pancreatitis group (10.73 ± 4.18 mg/dLv/s 3.909 ± 2.24 mg/dL.). Mean RANSON's score in severe pancreatitis group was highly significant compared to mild pancreatitis group (3.705 ± 0.77 v/s 1.98 ± 0.74). Most of the patients (75.9%) of mild pancreatitis group have RANSON's score ≤ 2, while all patients of severe pancreatitis group have score ≥3.Mean BISAP score in severe pancreatitis was highly significant in comparison to mild pancreatitis group (4.23±0.43 v/s 1.86±0.53). All patients of mild pancreatitis group have BISAP score ≤ 3 while all patients of severe pancreatitis groups have score ≥ 4.

Table 2: Sensitivity, specificity, Positive Predictive Value and Negative Predictive Value of MPV (at cut off value of 9.0 fl),CRP (at cut off value of 10mg/dl), RANSON's score(at cut off value of 3) and BISAP score(at cut off value of 4) to predict severity of acute pancreatitis

Statistic	MPV	CRP	RANSON's Score	BISAP score
Sensitivity	55.17%	90.91%	88.89%	100%
Specificity	98.59%	92.13%	67.86%	100%
Positive Predictive Value	94.12%	58.82%	47.06%	100%
Negative Predictive Value	83.34%	98.8%	95.00%	100%

In our study Sensitivity, Specificity, Positive Predictive value (PPV) and Negative Predictive value (NPV) of MPV (at the cut off value of 9.0fl) were 55.17%, 98.59%, 94.12% and 83.34% respectively; of S.CRP (at the cut off value of 10.0mg/dl) were 90.91%, 92.13%,58.82% and 98.8%, respectively ; of RANSON's score (at the cut off value of 3)were 88.89%,67.86%, 47.06% and 95.00%, respectively and of BISAP score (at the cut off value of 4) were 100%,100%,100%, and 100%, respectively to predict severity of acute pancreatitis.

Discussion

This prospective observational study of Comparative Evaluation of RANSON's Score, BISAP Score, S.CRP and MPV in prediction of severity of acute pancreatitis was conducted in the Department of Medicine, J.L.N. Medical College Ajmer.

According to Revised Atlanta Criteria 2012, AP is divided into three groups as mild, moderate and severe. Mild AP lacks local/systemic complications or organ failure and acute episode becomes milder or limits itself within a period less than 7 days. In AP with moderate severity, transient organ failure lasts for less than 48 hours or local complications (peripancreatic fluid collection, pancreatic necrosis) or systemic complications (exacerbation of a previously existing disease) are observed. In severe AP however, organ failure lasts for more than 48 hours

Inour study the mean age of patients of severe pancreatitis group was higher compared to mild pancreatitis group .We found more chances of severe AP with increasing age. Yilmaz Bilgic *et al.* and M. Orak. *et al* also found similar observations. Male gender was predominant in both mild pancreatitis group and severe pancreatitis group compared to female gender and this may be because of alcohol was the main etiology. In our study alcohol was the main etiology in both mild pancreatitis group (89.2%) and severe pancreatitis group (100.0%) followed by gall stone (10.8%). Jitin Yadav *et al* revealed alcohol as the main etiology (40.3%) followed by gall stone (31.1%) in patients of acute pancreatitis. In our study the mean glucose in severe pancreatitis group was significant compared to mild pancreatitis group (p=0.03)].P. Huang *et. al.* revealed highly significant mean glucose in severe pancreatitis group in comparison to mild pancreatitis group [218.92mg/dl v/s 135.32mg/dl (p<0.001)].Y I kibar *et al* revealed significant mean glucose in severe pancreatitis group compared to mild [159±29 v/s 143±45 mg/dl (p=0.029)] .

Mean total bilirubin was not significant when compared severe pancreatitis group to mild pancreatitis group [1.77±0.63mg/dl vs 1.45±0.66mg/dl (p=0.06)]. Yilmaz Bilgic *et al* revealed significant mean total bilirubin in severe pancreatitis groupin comparison to mild pancreatitis group [2.47mg/dl v/s 0.96mg/dl (p=0.007)] to predict severity.

In our study the mean AST was significant in severe pancreatitis group when compared to mild pancreatitis group to predict severity (p<0.01). Yilmaz Bilgic *et al* revealed than mean AST was significant in severe pancreatitis group in comparison to mild pancreatitis group [302 U/L v/s 108 U/L (p=0.001)]. P. Huang *et. al.* revealed that mean AST in severe pancreatitis was 108.55 U/L, while in mild pancreatitis the mean AST

was 95.44 U/L however this difference was not significant (p=0.645).Y I kibar *et al*. revealed highly significant mean AST in mild pancreatitis group compared to severe pancreatitis group [291±229 U/L v/s 112±57 U/L (p<0.001)].

There was no significant difference in mean ALT level in both groups in our study to predict severity. Yilmaz Bilgic *et al* revealed that the mean ALT was significant in severe pancreatitis group when compared to mild pancreatitis group [421 v/s 125 (p<0.001)].

Mean LDH level was highly significant in severe pancreatitis group in comparison to mild pancreatitis group to predict severity (p<0.001). Y. I. Kibar *et.al* and Yilmaz Bilgic *et al* both study also found similar findings.

There was no significant difference in mean amylase and lipase levels in both groups in our study to predict severity. Y. I. Kibar *et .al* and Yilmaz Bilgic *et al* both study also found similar findings.

In our study mean MPV in severe pancreatitis group was highly significant when compared to mild pancreatitis group (p=0.001). Peng Huang *et. Al* revealed highly significant mean MPV in severe pancreatitis group compared to mild pancreatitis group [11.54±1.49 flv/s 9.68±1.38fl (p<0.001)]. Y. Bilgic *et. al*. revealed that mean MPV in severe pancreatitis group (7.8fl) was lower as compared to mild pancreatitis group (8.1fl) however, this difference was not significant Our study revealed that the mean S.CRP level in severe pancreatitis group was highly significant when compared to mild pancreatitis group (p<0.001). Yilmaz Bilgic *et al*. revealed highly significant mean S.CRP levels in severe pancreatitis group in comparison to mild [9.6 v/s 2.0mg/dl(p=0.001). Y. I. Kibar *et al.*[70] showed that mean S.CRP level in severe pancreatitis group (10.7±10.0 mg/dl) was higher as compared to mild pancreatitis group (6.18±7.41 mg/L). However this difference was not significant.

In our study the mean RANSON's score in severe pancreatitis group was highly significant when compared to mild pancreatitis group [3.705±0.77

v/s 1.98±0.74 (p<0.001)]. P. Huang *et. al*. revealed highly significant mean RANSON's score in severe pancreatitis group compared to mild pancreatitis group[4.76±1.50 v/s 3.07±1.90 (p<0.001)]. Yilmaz Bilgic *et al* revealed significant mean RANSON's score in severe pancreatitis group compared to mild pancreatitis group [3 v/s 2 (p=0.002)].

In our study the mean BISAP score in severe pancreatitis group was highly significant in comparison to mild pancreatitis group [4.23±0.43 v/s 1.86±0.53 (p=0.001)]. J.L. Pednekar *et al*. showed statistically significant trend for increasing mortality with increasing BISAP score (p<0.001). J. H. Cho *et. al*. revealed that the mean BISAP score in severe pancreatitis was 1.90, while in mild pancreatitis the mean BISAP score was 1.

In our study MPV (at cut off value of 9 fl) was less sensitive but highly specific to predict severity of acute pancreatitis. Peng Huang et al. revealed Sensitivity Specificity, PPV and NPV of MPV(at the cut off value of 12 fl) were 44.8%,90.6%, 87.8% and 82.1% respectively to predict severity of acute pancreatitis.

In our study S.CRP (at cut off value of 10mg/dl) was highly sensitive & specific to predict severity. Aaron D Stirling *et al*. revealed Sensitivity, Specificity, PPV and NPV of CRP (at the cut off value of 190mg/dl) were 83.3%, 69.5%, 31.7% and 96.1% respectively to predict severity of acute pancreatitis. Chen CC *et al* revealed the sensitivity and specificity of CRP in predicting a severe attack were 94% and 76 %, respectively (at the cut off value of 8mg/dl) to predict severity of acute pancreatitis. Ajay K Khanna et al. revealed Sensitivity, Specificity, PPV and NPV of CRP(at the cut off value of 150mg/dl) were 86.2%, 100%, 100% and 88.6%, respectively to predict severity of acute pancreatitis.

Our study showed that RANSON's Score (at cut off score of 3) was significantly sensitive but less specific to predict severity. Various studies showed different Sensitivity, Specificity, PPV and NPV of RANSON's score (at the cut off value of

3) to predict severity. A H Kumar et al ,Ji Young Park et al, Jitin Yadav *et al* and Ajay K Khanna *et al* found the Sensitivity, Specificity, PPV and NPV were 80%, 96.55%, 88.89% and 93.33% ; 74.2%, 71.3%, 22.8% and 96.0%; 97.6%, 93.5%, 89.1% and 98.6% ; 83.9%, 78.0%, 74.3% and 86.5%, respectively to predict severity.

In our study BISAP Score (at cut off score of 4) have very high sensitivity and specificity to predict severity along with very high PPV and NPV. Sensitivity, Specificity, PPV and NPV of BISAP score showed by Ji Young Park et al (at cut off score of 2) were 71%, 84.9%, 34.9% and 96.3%, respectively; by Jitin Yadav *et al* (at cut off score of 3) were 97.6%, 94.8%, 91.1% and 98.6% respectively ; by Ajay K Khanna *et al* (at cut off of 2) were 74.2%, 68.3%, 63.4% and 77.8% respectively ; and A H Kumar, et al (at the cutoff of 3)were 90.91%, 86.67%, 71.43% and 96.30%, respectively to predict severity of acute pancreatitis.

When we compare all four markers (MPV, S.CRP, RANSON's score and BISAP's score), BISAP's score was best to predict severity of acute pancreatitis (at cut off value of 4) in comparison to other three markers. S.CRP and RANSON's score was equally sensitive to predict severity but better than MPV.

MPV and S.CRP were nearly equally specific to predict severity but their specificity were higher than that of RANSON's score. PPV of MPV was very high in comparison to S. CRP and RANSON's score to predict severity. NPV of S. CRP and RANSON's score were nearly equal to predict severity, and both have better NPV then MPV.

Conclusion

MPV, S.CRP, RANSON's score and BISAP score, all four markers can be used to predict the severity of acute pancreatitis. BISAP score was found to be the best predictor of severity of acute pancreatitis among all four markers. BISAP score equal to or greater than 4 invariably indicates severe acute pancreatitis. Prognostic accuracy of RANSON's score and S.CRP is better than MPV in terms of sensitivity but less sensitive and specific than BISAP. MPV is also a good prognostic marker in terms of its specificity and easy availability in prediction of severity of acute pancreatitis.

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