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"TO STUDY THE MORTALITY PREDICTION OF ICU PATIENTS WITH PERFORATION PERITONITIS, REQUIRING EMERGENCY LAPAROTOMY''

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Abstract

Introduction- Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. It's the primary cause of death from infection, especially if not recognized and treated promptly. It's a syndrome caused by pathogen factors and host factors with characteristics that evolve over time. What differentiates sepsis from infection is an aberrant or dysregulated host response and the presence of organ dysfunction. The clinical and biological phenotype of sepsis can however be modified by preexisting acute illness, long-standing co-morbidities, medication, and interventions.

Aims and objectives- ''to study the mortality prediction of ICU patients with perforation eritonitis, requiring emergency laparotomy''

Methods and materials- This is a prospective cohort study done in a tertiary care center in central India ''

conducted in the department of General Surgery Department of Surgery in people's college of medical science and research Centre, Bhopal for two-year study in 50 patients. Surgical Abdominal Sepsis admitted in surgical intensive care unit (SICU) during study period, for two years.

Inclusion criteria– All the patients ≥16 years of age admitted in SICU, as a result of perforation peritonitis requiring exploratory laparotomy and willing to participate in the study after written informed consent were included. Age<16years and patient with Sepsis secondary to trauma, Laparotomies for non-septic indications are excluded from study.

After obtaining Ethical clearance from Institute's Ethical Committee, all the patients fulfilling the inclusion criteria were enrolled in the study. Written consent was obtained from all the study participants. The participants were divided in two groups i.e. survivors and non survivors based on their outcome.

Results- -Mean age of patients in present study was 36±16.14 years. In the present study 42(84%) out of 50 patients were males while 8(16%) were females. All 5 patients who died were males. Most common etiology of SABS was small intestine perforation (36%) followed by gastric perforation (26%). Mean Apache score was maximum in intra-abdominal abscess (105) followed by ischemia (57) and gastric perforation and was minimum in large intestine perforation (29.3). Mean of MAP of 45 patients in survivor group was 82.55 mmHg while the same in non-survivors was 75 mm Hg. Mechanical ventilation was used in total of 3 patients, out of which 1 survived and 2patients succumbed to death. The association of mechanical ventilation usage with mortality (chi square test) amongst survivors and non survivors was found to be statistically significant (p=0.0008).

Deranged Sodium was seen in 11 out of 45 survivors (24.4%) and 2 out of 5(40%) non-survivors. The survivors had a mean urine output of 1020 ml and non-survivors had a mean urine output of 350 ml. In case of serum creatinine; mean of survivor group was 0.98 while in non-survivors is1.74. Mean albumin in survivor group was 3.09mg/dl and in non-survivors was1.94. In present study, 12 patients had APS score less than 30 with no mortality. 1 out of 31 patients in 30-60 score range died while 4 out of 7 died in case of score >60. A receiver operating characteristic (ROC) curve, comparative analysis of the mortality predictions with APACHE IV is done and shows AUC =0.911 and p <0.001. Thus, shows the high predictive efficacy of APACHE IV score. The mean observed length of stay of all patients was 6.65 days against an expected LOS (length of stay) of 4.6 days. Overall O:E Ratio was 1.44 against O:E of 1.21 in non-survivors with observed and expected LOS of 10.2 and 8.42 days. The difference was statistically significant with p value =0.02.

Conclusion- From this study we concluded that, results in terms of Length of stay are not accurate and a further work upon the same is required. Results of the study may be improved if sample size was bigger.
Hence, a larger study with greater sample size and if possible, involvement of multiple centers is recommended which could help in reaching some conclusive and milestone results.

From this study we evaluate the mortality of ICU patients with perforation peritonitis requiring emergency laparotomy, which is essential for all healthcare workers.

Keywords- SICU, emergency laparotomy, perforation peritonitis.

Introduction-

APACHE (Acute Physiology and Chronic Health Evaluation) score is one of the several intensive care unit (ICU) scoring systems. The death rate of patients admitted to ICU's is much higher than that of other areas.

APACHE has two components: Acute Physiology Score (APS) and the chronic health evaluation, which incorporates the influence of co-morbid conditions (such as diabetes and cirrhosis).Out of these, physiological scoring is aimed at measuring the immediate status of the patient and focuses on the vital organs and their functional evaluation. It is a reflection of long-term disease process. Results of the evaluation can be used to estimate the mortality rate for patients in the ICU and during the hospitalization. [1]

SURGICAL ABDOMINAL SEPSIS (SABS)[6]Defined as patients with evidence of preoperative severe sepsis or septic shock with a suspected or known abdominal source of infection requiring laparotomy for source control.

Severe Sepsis is defined as meeting at least one of the following criterions of SIRS with evidence of organ dysfunction.[7]

• TEMPERATURE>38°C or<36 °C
• HR>90/minute
• RR>20 /minute or$PaCO_2$<32mm Hg
• WBC Count>12,000 cells/mm^3 or<4,000 cells/mm^3or>10%immature bands.
• Evidence of Organ dysfunction
• Hypoperfusion [Lactate>1mmol/L]
• Hypotension [SBP <90mmHg]

Aim and objectives-
This is a prospective cohort study done in tertiary care center in central India ''**To study the mortality prediction of ICU patients with perforation peritonitis, requiring emergency laparotomy''** was conducted in Department of Surgery in people's college of medical science and research Centre Bhopal for two-year study in 50 patients, Surgical Abdominal Sepsis admitted in Surgical intensive care unit (SICU) during study period, for two years periods

Inclusion criteria–
All the patients≥16 years of age who were admitted in SICU with perforation peritonitis requiring exploratory laparotomy. Patients willing to participate in the study after written informed consent were included.

Exclusion criteria-
• Age<16years
• Sepsis secondary to trauma
• Laparotomies for non-septic indications

Methodology-
After obtaining Ethical clearance from Institute's Ethical Committee, all the patients fulfilling the inclusion criteria were enrolled in the study. Written consent was obtained from all the study participants. Physiological data and Biochemical data were collected at the time of admission or within24 hours of admission.

The variables used included age, sex, dates of admission, discharge or death, systolic and diastolic blood pressure, body temperature, heart rate, respiratory rate, glucose, blood urea nitrogen, serum sodium, creatinine, blood hematocrit, white blood cells, serum albumin and bilirubin, urine output during the first 24 h of ICU admission, pH, fraction of inspired oxygen, partial pressure of carbon di oxide and partial pressure of oxygen.

Death or discharge and length of stay in ICU were followed up by referring to patients' medical records. Additionally, APACHE-IV score, Glasgow coma score (GCS), and acute physiology score (APS)were calculated by APACHEIV calculator. (Online tool)

The present study enrolled 50 patients and the participants were divided in two groups i.e. survivors and non survivors based on their outcome.

Data was compiled using MS excel and comparison of APACHE IV score was made between the two groups (survivors and non-survivors) and its predictive efficacy was analyzed.

Statistical analysis-
APACHE scores and outcome variables were compared between survivors and non-survivors using Student's t-test/Fischer exact test wherever applicable. Data Analysis was done using SPS Software.

The present study enrolled 50 patients fulfilling inclusion criteria during the study period. The patients

were observed during hospital stay until final outcome i.e. discharge or death. On the basis of their final outcome i.e. survival; patients were divided in two groups: -survivors and non-survivors.

In 2016, the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)[8]were released according to which, SIRS(Systemic Inflammatory Response Syndrome) is defined as the presence of Two or more of:
• Temperature>38°Cor<36°C
• Heart rate>90/min
• Respiratory rate >20/min orPaCO2 <32 mmhg.
• WBC count > 12000/mm3 or <4000/mm3 or >10% immature bands

Prediction Scores-
Scoring systems have been developed in response to an increasing emphasis on the evaluation and monitoring of health services. These systems enable comparative audit and evaluative research of intensive care. The ideal components of a scoring system should comprise of data collected during the course of routine patient management that are easily measured, objective, and reproducible. Scoring systems, developed in the 1980s are applicable to heterogeneous groups of critically ill patients.

The evaluation of severity of illness in the critically ill patients is made through the use of severity scores and prognostic models. Severity scores are instruments that aim at stratifying patients based on the severity of their illness, assigning to each patient an increasing score as their severity of illness increases. Prognostic models, apart from their ability to stratify patients according to their severity, predict a certain outcome(usually the vital status at hospital discharge) based on a given set of prognostic variables and a certain modeling equation.[20]

Types of ICU outcome scoring systems Specific[21]

1.Head injury	Glasgow coma score
2.Burns	%+age~ mortality
3.Trauma	Injury severity score (ISS)trauma score
4. IHD	NYHA/AHA classification
5.Pancreatitis	Ranson's scoring criteria
6.Liverfailure	Child Pugh classification, MELD Score, PELD Score

1. Anatomical Scoring– Depends on the anatomical area involved.

• Useful for trauma audits and research e.g. Injury Severity Score (ISS), Abbreviated Injury Score (AIS).

2. Therapeutic Scoring– Based on type and amount of treatment received.

• Sum of weighted scores of therapeutic interventions, Correlates well with outcome, Wide applicability. e.g. Therapeutic Intervention Scoring System (TISS)

3. Physiological–Based on degree of derangement of routinely measured physiological variables. Designed for quality review rather than prognosis e.g. Acute physiology and chronic health evaluation (APACHE), Simplified Acute Physiology Score (SAPS).

Specific models[24]

First generation	APACHE I
Second generation	SAPS IMPMI APACHE II
Third generation	SAPS II MPMIIAPACHEIII
Fourth generation	SAPS IIIMPMIII APACHEIV

Organ dysfunction scores-[25]

To risk-adjust patients with longer, more severe illnesses like sepsis and acute respiratory distress syndrome, several models of organ dysfunction or failure have become available, including the

• Multiple Organ Dysfunction Score (MODS),
• Sequential Organ Failure Assessment (SOFA),
• Logistic Organ Dysfunction Score (LODS)

Sequential Organ Failure Assessment (SOFA)-[26]

Previously known as Sepsis related Organ failure assessment, The Sequential Organ Failure Assessment (SOFA) score was developed to quantify the severity of patients' illness, based on the degree of organ dysfunction, was introduced in 1994 and further revised in 1996.

The SOFA score is composed of scores from six organ systems, each graded from 0 to 4 points according to the degree of dysfunction, giving a possible score of 0to 24. The SOFA scoring system takes into account the time course of a patient's condition during the entire ICU stay.

Organ dysfunction can be identified as an acute change in total SOFA score ≥2 points consequent to the infection. The baseline SOFA score can be assumed to be zero inpatients not known to have preexisting organ dysfunction.

ASOFA score ≥2 reflects an overall mortality risk of approximately 10% in a general hospital population with suspected infection.[27]

Observation and results-

-Mean age of patients in present study was 36±16.14 years. Out of total 50 patients, 7patients belonged to less than 20 years of age, with no mortality. 33 patients belonged to 20-50 years of age group with 3 deaths and 10 patients belonged to more than 50yearswith 2 deaths.

-Inpresentstudy,42(84%) outof50patientswere maleswhile8(16%) were females. All 5 patients who died were males.

-Most common etiology of SABS was small intestine perforation (36%) followed by gastric perforation (26%), Small intestinal obstruction (14%), appendicular perforations (8%), large bowel perforations (6%), large bowel obstructions (4%) and intra-abdominal abscess (1%). Mean Apache score was maximum in intra-abdominal abscess (105) followed by ischemia (57) and gastric perforation and was minimum in large intestinal perforation (29.3).

Table1 Etiological Breakup of Diseases with Mortality

Etiology	No ofPatients	Survivors	Non-survivors	Mean ApacheScore
LargeIntestinePerforation	3(6%)	3	0	29.3
SmallIntestinePerforation	18(36%)	18(100%)	0	43
GastricPerforation	13(26%)	10(76.92%)	3(23.07%)	50.4
Abscess(Intra-abdominal)	1(2%)	0	1(100%)	105
AppendicularPerforation	4(8%)	4(100%)	0	43.5
LargeIntestineObstruction	2(4%)	2(100%)	0	34
SmallIntestineObstruction	7(14%)	7(100%)	0	35
Ischemia/Infarction	2(4%)	1(50%)	1(50%)	57

-Mean of MAP of 45 patients in survivor group was 82.55 mm Hg while the same in non-survivors was 75 mm Hg. Test of significance could not be applied as the data in the two groups was less.

Table2 MAP values in survivors and non survivors

	No of Patients	MAP(mmHg)
Survivors	45	82.55
Non-Survivors	5	75

Table3 Use of Mechanical Ventilation in Survivors and Non-Survivors

MechanicalVentilationUsed	Survivors	Non-Survivors
Yes	1	2
No	44	3
P=0.0008		

-Mechanical ventilation was used in total of 3 patients, out of which 1 survived and 2 patients succumbed to death. The association of mechanical ventilation usage with mortality (chi square test) amongst survivors and non survivors was found to be statistically significant(p=0.0008).

-Deranged Sodium was seen in 11 out of 45 survivors (24.4%) and 2 out of 5(40%) non-survivors. The association of mortality with deranged sodium level using chi square test was found to be statistically insignificant in present study(p=0.45)

Table4 Sodium levels in survivors and non-survivors

Sodium level	Survivors	Non-Survivors
Hypo/Hypernatremia	11	2
Normal Na+	34	3
PValue=0.45		

-While the survivors had a mean urine output of 1020 ml and non-survivors had a mean urine output of 350 ml. Test of significance could not be applied as the data was less.

Table5 Mean Urine output comparison in survivors and non-survivors

	Noof patients	MeanUrineoutput
Survivors	45	1020
Non-Survivors	5	350

-In case of serum creatinine, mean of survivor group was 0.98 while in non-survivors is 1.74. Test of significance could not be applied as the data was less.

Table6 Serum Creatinine comparison in survivors and non-survivors

	No of patients	Mean Serum Creatinine
Survivors	45	0.98
Non-Survivors	5	1.74

-Mean albumin in survivor group was 3.09mg/dl and in non-survivors was 1.94. Test of significance could not be applied as the data was less.

Table7 Serum Albumin in Survivors and non-survivors

	No of patients	Mean Serum Albumin
Survivors	45	3.09
Non-Survivors	5	1.94

APS Score-

-In present study,12 patients had APS score less than 30 with no mortality.1out of 31patients in 30-60 score range died while 4 out of 7 died in case of score >60.

Table9 Division of cases on basis of APS score

APS Score	Total Patients	Mortality
<30	12	0
30-60	31	1
>60	7	4

Estimated Mortality Rates

-A receiver operating characteristic (ROC) curve, comparative analysis of the mortality predictions with APACHE IV was done and shows AUC =0.911 and p <0.001. Thus, shows the high predictive efficacy of APACHEIV score.

Length of Stay(LOS)-

-The mean observed length of stay of all patients was 6.65 days against an expected LOS (length of stay) of 4.6 days. Overall O:E Ratio was 1.44 against O:E of 1.21 in non-survivors with observed and expected LOS of 10.2 and 8.42 days. The difference was statistically significant with p value =0.02

Table10Comparison of Observed and Expected LOS

NoofPatients	Observed LOS(Days)	Expected LOS(Days)	O:ERatio
50	6.65	4.6	1.44
5(non-Survivors)	10.2	8.42	1.21
Pvalue0.0270			

Discussion-

The present study entitled "**Evaluation of Predictive Efficacy of ApacheIV Score in Surgical Abdominal Sepsis"** was conducted on 50 patients admitted in S.I.C.U. diagnosed with Surgical Abdominal Sepsis requiring exploratory laparotomy. Mean age of patients in our study was 36±16.14years. 33 patients belonged to20-50years of age followed by 10 patients of >50 years of age and 7 patients of <20 years of age. Mortality was observed in 2 and 3 patients belonging to >50 years and 20-50 years of age group respectively. There was an age-wise increase in the rate of mortality as in the results above but the relation was not found to be statistically significant. Similar findings were seen in the study by **MosesS et al.** who also had similar results.[1] In another study by **ChanT etal,** the mean age of study participants was 62.8±15.2 years. They found a significant difference in age between survivors(60.7years,95%CI58.3,63.2) and non-survivors(67.9years,95% CI64.1,71.6).[32]

Majority of participants in present study were males that is 84% while only 16% participants were females. Mortality was observed in 5males in our study. In a study by **Ghorbani M et al** in Iran, study population comprised of 53.9% males and 46.1%females.[33]In another study by **Shoukat H et al** 55.5% and 44.5% participants were males and females respectively. Out of 86 male patients, mortality occurred in 41(47.67%) patients and did not occur in 45 (52.33%) patients, while 69 patients were females in which mortality occurred in 31(44.92%) and not in 38 (55.08%) patients.[38]

Most common etiology observed in present study was small intestine perforation (36%), followed by

gastric perforation (26%) and Small intestinal obstruction (14%).

Similar disease patterns were found in the study by **Vishwani et al**[39]and **Shoukat Hetal**[38], both of which included patients of sepsis undergoing exploratory laparotomy.

In present study, based on mortality, patients were divided into 2 groups, survivor and non survivor. Mean of MAP of 45 patients in survivor group was 82.55 mm Hg while the same in non-survivors was 75 mm Hg. Not much studies have considered mean arterial pressure. The abdominal perfusion pressure (mean arterial pressure– intra-abdominal pressure) has been shown to correlate with survival when maintained at levels greater than 50 mm Hg to 60 mm Hg, but level I evidence examining this as an endpoint of resuscitation has yet to be obtained.[40]

In present study, mechanical ventilation was used in 3 patients. The association of mechanical ventilation usage with mortality amongst survivors and non survivors was found to be statistically significant (p=0.0008). **Martin ND et al** in their study could not assess the association of mechanical ventilation and mortality, since mechanical ventilation was required in all patients.[41]

The present study observed insignificant association of mortality with deranged sodium level. The mean urine output among survivors was 1020 ml and that in non-survivors was 350 ml. In case of serum creatinine, mean of survivor group was 0.98while in non-survivors is 1.74. Mean albumin in survivor group was 3.09 mg/dl and in non-survivors was 1.94. Test of significance could not be applied as the data was less. The development of Acute Kidney injury is common following laparotomy, reaches greatest prevalence 48 h after initial laparotomy, and is an independent predictor of increased mortality.[42]

In present study it was observed, higher the Apache score, worst is the prognosis and more the mortality. Test of significance showed statistically significant association between mortality and Apache score (p<0.0001). **Ghorbani M et al** also observed significant difference in mean Apache score amongst survivors and non survivors(p<0.001).[33]**El-Naggar TA et al** in their study observed APACHE IV scores were significantly higher between dead than alive patients on admission and after 48 h, but were not able to predict death in ICU.[43]**Chan T et al** suggested APACHE-IV crudely distinguished between survivors and non-survivors.[32]

Also present study observed higher the Apache score, worst the prognosis and more the mortality. These findings were similar to study by **El-Naggar TA et al**[43] and **Saleh A et al**. [44]**Yamin S et al** in their study observed mean APACHE IV score of survivors to be 54.55, while mean APACHE IV score of non survivor was 85.07which was significantly higher. 63.9% patients had APACHE IV score <60, out of these 14.8% didn't survive. 27.8% patients had APACHE IV score >81 out of these65.8% didn't survive (p<0.001). The 62.1% of overall population show the same outcome as predicted by APACHEIV (p=0.61).[45]

The ROC curve showed the results to be pretty accurate with an AUC=0.91andp <0.01.AUC was 0.93 in a study in Turkey by **Ayazoglu TA et al.**[46]In a study In South Korea also, AUC was 0.80 and significantly better than its predecessors.[47]**Zimmerman JE et al** concluded APACHE IV had good discrimination (area under the receiver operating characteristic curve = 0.88) and calibration (Hosmer-Lemeshow C statistic = 16.9, p = .08). For 90% of 116 ICU admission diagnoses, the ratio of observed to predicted mortality was not significantly different from1.0.[28]

Kuzniewicz MW etal also found similar results. They observed APACHE IV had the best discrimination (area under the receiver operating characteristic curve [AUC],0.892) compared to MPM(0)III(AUC,0.809),and SAPSII(AUC,0.873;p<0.001).

In terms of Length of stay (LOS), Mean of all patients was 6.65 days against an expected LOS of 4.6days. Overall O:E(ObservedLOS:ExpectedLOS) Ratio was 1.44 against, O:E of 1.21 in non-survivors with observed and expected LOS of 10.2and 8.42 days. The results were pretty accurate with higher accuracy in non-survivor than the survivor group. The slightly higher prediction of Length of stay in survivor group by APACHEIV may be because of a conservative approach to shift and discharge patients in the institute because most patients were from the rural and low socio-economic group and hence the patient factors have to be kept in mind.[49]

In a pilot study predicting ICU length of stay using APACHE-IV in severe sepsis patients by **Chattopadhyay and Chatterjee in Cleveland**, Ohio, similar results was found with a significant over-prediction of length of stay.[50]

Lack of inpatient bed availability is a major contributor to emergency department(ED) crowding. Important reductions in LOS at ED (and others) and smoothening of ambulance diversion occur in urban academic medical center after an increase in adult ICU beds. A recent study demonstrated that the most notable change after ICU expansion was a decrease in time spent on ambulance diversion. Increasing ICU beds appears to have shortened ED LOS for ICU patients but has less effect on other admitted patients and apparently, no effect on patients discharged home. In emergency care a perfect balance between given resources and demand is much more difficult to achieve and maintain. In reality, certain key resources, e.g. ICU beds, are often over-utilized.[18]

Conclusion-

From this study we concluded that, results in terms of Length of stay are not accurate and a further workup on the same is required. Although, the results may be improved after removing the limitation of the study i.e. small sample size.

Hence, a larger study with greater sample size and if possible, involvement of multiple centers is recommended which could help in reaching some conclusive and milestone results.

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