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Diagnostic Utility of Procalcitonin and Crp in the Detection of Bacterial Infection in Patients of Abdominal Sepsis

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Type of Article- Study Protocol
Conflict of Interest: None

Abstract:

Background: Abdominal sepsis presents as systemic inflammatory response of the host to bacterial peritonitis which results due to direct spillage of luminal contents into peritoneum .Postoperative bacterial infections, is a one of the causes of morbidity after abdominal surgery.CRP is an acute phase protein that is released during inflammatory conditions.Standard concentrations of C reactive protein are from 0.8 mg/dl to 3.0 mg/l in healthy individuals. However at 10 mg/l some healthy adults may exhibit elevated C reactive protein levels.CRP levels rise to about 10.000 fold from less than 50 micro gram/litre to more than 500 mg/l when there is stimulus. It doubles every 8 hours peaking 30 to 50 hours after an injury or inflammation. Because of bacterial infection CRPs between 100 and 500 mg/l are considered highly predictive of inflammation.Procalcitonin is a precursor peptideto the hormone calcitonin.The amount of procalcitonin is below the limit of detection (0.01 microgram/lit) in the bloodstream of healthy individuals . In response to pro inflammatory stimuli which is mostly of bacterial origin , the amount of procalcitonin increases. The procalcitonin induction duration is 4-12 hours with a half-life of 22 to 35 hours . With extreme infection triggered by inflammatory cascade and systemic reaction, the levels of procalcitonin in blood increase, correlating it with severe disease.

Objectives:

1. To evaluate diagnostic utility of C-reactive Protein in detection of bacterial infection in abdominal sepsis.

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2. To evaluate diagnostic utility of procalcitonin in detection of bacterial infection in abdominal sepsis.

Methodology:It will be a prospective study done on the patients affected with acute abdomen. It will be conducted at department of general surgery, JNMC and AVBRH, Sawangi (Meghe), Wardha of DMIMS (DU) .The study will be done on patients affected with acute abdomen.

Results: The result would be undertaken in SPSS software

Conclusion: Conclusion will be based on findings for study of protocol

Keywords: Procalcitonin, C- Reactive Protein (CRP), Sepsis

INTRODUCTION:

In these modern times, it is a necessity to recognize, that treatment of patients with abdominal sepsis is the basic problem in surgical fields owing to the invariably high mortality rates. Early diagnostics and targeted therapies are the key points in order to improve the outcomes in septic conditions. The biomarker is a laboratory parameter that could be calculated consideratelyand defined as a predictor of standard and pathological biological processes [1] .In seriously ill patients sepsis remains as one of the major causes of death, despite all the efforts to improve patient's life. It results from direct spillage of the contents in the intestinal lumen into the peritoneal space. For primaryidentification of sepsis, biological markers could help medical practitioners to differentiate between septicaemia and immune responsiveness to inflammation. Generally the markers are seen to utilized in risk identification, diagnosis, monitoring of management, result, and outcome identification [2] .

Septicaemia is an atypical response of the body to what in usual times is normal infection, and it generallyexhibits a path of reaction by the individual's immune system to infection. Post a hyper-inflammatory reaction there is an immunocompressivetime phrasewhile which multiple organ disorder is found and the individual is bound to develop nosocomial infection. Biomarkers to recogniseinfection may aid inprior management which, even though essentially conservative, can lessen the risk of death. Even though lactate is currently the most often used biomarker in recognition of sepsis, other biomarkers may easeinintensifying of lactate's usefulness; these include markers of the hyper-inflammatory phase of sepsis, like pro-inflammatory cytokines and chemokines, proteins produced by infection and inflammatory response such as c- reactive protein and procalcitonin and neutrophil and monocyte activation factors. These days, markers of the immunocompressive phase of sepsis, such as anti-inflammatory cytokines, and alterations of the cell surface markers of monocytes and lymphocytes have are beingstudied. Coexistenceof proalong with anti-inflammatory biomarkers in a multi-marker panel can help inidentification ofindividuals who are goinginto severe sepsis prior multiple organ disorder havinggone too far. In conjunctionoldenways to management that affect the immunocompressive phase, these biomarkers could help in reducing the mortalityconcerned withsevere sepsis which, despite of recent advances, remains elevated.

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The use of biomarkers has been used for screening and diagnosis for a few years, Biomarkers are already available for early detection of worse prognostic conditions and factors with increasedcomparison with clinical graveness and their utilisation as risk and prognostic markersare promising. Sepsis in seriouslysickindividuals is aimportantreason of mortality and morbidity. For seriously ill individuals the most frequently used biomarkers are CRP and Procalcitonin.

Clinical judgement is still the most widely usedsystem in decidingbeginning of antibiotic course in patients. Clinical assessment becomes more nonspecific over the course of multiple infectious diseases and often begins too late to establish a basis for when to begin the antimicrobial management. Also microbiological diagnosis achieved by isolation of causative pathogen is not always possible, microbiological criteria is of little help due to delay in culture results, interference with bacterial growth, difficulty in obtaining samples or because bacteriological evidence may not develop on clinically symptomatic stage. In this context biomarkers play a key role. Various studies have shown that the measurement of both PCT and CRP play a key role in possibly reducing the duration of antibiotics which eventually contributes in reducing bacterial resistance.

CRP is seen to be accepted for a while now as anonspecific acute phase reactant protein which increases 4-6 hours after subjection to inflammatory stimulus.Accepted levels of C reactive protein are seen to be between 0.8 mg/litre to 8 mg/litre in healthy persons. but it is seen that, some healthygrown-ups show elevated CRP at 10 mg/L. CRP levels are also found to be raised with age, mostly due to the existence of other comorbid conditions. There are no seasonal variations of CRP levels [3]. CRP between 100 and 500 mg/L is seen to be mostly due to the existence of inflammation due to bacterial infection. Once inflammation is seen to be receded, due to its relatively short half-life the C reactive proteinlevels in blood decreasesimmediately [4].

Findings in seriously sick people, mainly the individuals with serious community acquired pneumonia, have shown that, as a prognostic measure, tracingconsecutive c- reactive protein levels and their difference in reaction to antibiotic treatment over the first 5-7 days of clinical examination is of superior gain than utilising just absolute numbers. Bearing in mind that CRP levels have already been largely used in clinical use for ages and that they can be gotten with simpleapproach and less cost and are seen in allmedical careprovisions, CRP is established as a major biomarker of reaction to antibiotic therapy when calculatedintensely. This particular analysis hence warrants a much alikeexamination in young individuals; such examination has already been submitted, albeit preliminarily.

Though C Reactive protein is seen to be one of the moststudied biomarkers for ages its proper utilisation along with clinical examination and clubbed up with other biomarkers is of utmost importance and could be taken into consideration systematically in intervention and management of sepsis

PCT is a calcitonin receptor that is secreted in healthy people by thyroid gland neuroendocrine c-cells, with limited serum levels in these cases. PCT however is secreted

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during systemic infection causing to its increase in serum levels allowing it to bedependable to distinguishin sepsis and non-infectious systemic inflammatory response syndrome [5]. Bacterial infections causeaoverall increase in the CALC-1 gene expression and liberation of PCT (>1 μg/mL) [6]. Computation of procalcitoninwould aid as a hallmark of critical sepsisdue to bacteria and would be supportive in general grades well with the magnitude of sepsis, even though it is said that levels of procalcitonin in the blood are rarely seen [7].Procalcitonin is also said to be seen deciding the prescribing of antibiotic therapy since its levels are impeded by IFN-gamma in viral infection and its amount correlate with presence of bacterial infection .Procalcitoninimmediately increases in 3 to 6 hours resulting in bacterial infection proving the capacity to distinguish between localised and systemic infections.

Scrutiny on serial PCT calculations when patient first gets admitted and through complete hospital stay have been carried out to compare this biomarker with disease magnitude, multiple organ dysfunction, and death. These studies indicate that serial PCT calculations are seen a possible testification of patient outcome.

Very less proof is available with the use of procalcitonin as a biomarker.A new prospective single centre longitudinal study of 62 young individualsfound to have SIRS and sepsis revealed raised PCT values observed in individuals with paediatric logistic organ dysfunction (PELOD) scores higher than or measuring sameas 12 than in individuals with values less than 12 within initial 5 days of admission in hospitals.The researchconvey that procalcitonin levels were related to magnitude of infection and organ failure in patients of sepsis.

The systemic inflammatory reaction of the host to bacterial peritonitis is abdominal sepsis, resulting due to direct spillage of luminal material into peritoneum . Postoperative bacterial infections, is a one of the causes of morbidity after abdominal surgery.

Sepsis is life threatening and aids largely to mortality rates of critical care units. Sepsis willlead to multiple organ dysfunction and septic shock without properfollow-up. Sepsis is identified as life threatening organ dysfunction stimulated by person's reaction to infection that is impaired [8]. It is a worldwide health-care concern characterised by inflammation that leads to organ dysfunction in response to microbial infection. If initial treatment is delayed sepsis is characterised as an infectious systemic inflammatory response associated with elevated morbidity and mortality rates. Numerous biomarkers (interleukins [IL]-2 and IL-6 and tumor necrosis factor-α), leukotrienes, acute-phase proteins C-reactive protein , and adhesion molecules, are beingstudied with differentresults, detecting and directing the severity of sepsis. These days, procalcitonin (PCT) has been used as noble marker found to help in direct clinical opinion making in sepsis treatment.

Above mentioned research is intended to see the efficacy of PCT and CRP as diagnostic markers of sepsis and correlate these biomarkers in tertiary care hospitals with blood culture, parameters and scores of sepsis. PCT and CRP are both revolutionary laboratory markers that have in modern times proved to be useful worldwide.

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METHODOLOGY:

It will be a prospective study done on the patients affected with acute abdomen. It will be conducted at department of general surgery, JNMC and AVBRH, Sawangi (Meghe), Wardha of DMIMS (DU) .

The study will be done on patients affected with acute abdomen. The study is going to be a prospective study which will be carried out in a group of 120 people. Informed consent will be obtained from all patients and institutional ethical committee approval DMIMS (DU) approval will be taken.

• **StudyDesign**: Prospective Study

• **Study Setting**: AVBRH, Sawangi (Meghe), Wardha

• **Sample Size :**120 patients

Sample Size Calculation (With Desired Margin Of Error)

$N= Z_{\alpha/2}^2 .P(1-P)/ d^2$

Where,

$Z_{\alpha/2}^2$ – level of significance at 5% i.e, 95 % confidence interval = 1.96

P= prevalence of ecoli= 17.91 %=0.1791

D= desired error of margin = 7% = 0.007

$n = 1.96^2 x 0.1791 x (1-0.1791)/ 0.07^2$

= 115.26

120 patients needed in the study

Group A – Patients managed surgically

Group B – patients managed non surgically

Inclusion Criteria :

All the patients coming to AVBRH for all non-surgical and surgical abdominal cases like -

- Cholecystitis
- Choledocholithiasis,
- Gastric perforation,
- Small bowel perforation,
- Large bowel perforation,

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- Appendicitis,
- Perforated appendicitis
- Abdominal abscess.

Exclusion Criteria :

- Patients coming in diagnosed with abdominal sepsis already and undergoing treatment.
- Small and Large bowel malignancies.
- Abdominal Koch.
- Laparoscopic Surgeries
- Conditions not mentioned in the inclusion criteria

Analysis :

Analysis will be done with intention to treat principles. All participants with available data at baseline and follow up visits will be included. The impact of missing values will be explored in sensitivity analysis. The data will be entered into the Excel spread sheets and statistical analyses will be conducted using SPSS software. Descriptive analyses of age, sex, and treatment compliance will be performed. The histogram will be plotted to observe the distribution of all the variables and continuous variables which are normally distributed will be described using mean and standard error. The effect size will be expressed in terms of relative risk and risk difference along with their 95% confidence interval.

Expected Outcomes/ Results:

This study of biomarkers can be effective in detection of bacterial infection in various causes of abdominal Sepsis.

DISCUSSION :

According to Ravi S Samraj et al. biomarkers provide a method for encouraging early identification, in recognising the patient populations at increased risk of complications, and in tracking the disease progression, which are important assessments for successfulmanagement and optimizing in health outcomes of the patient.

According to Xiao Z et al. persistent elevation of CRP and PCT levels in vlood can be correlated with presence of sepsis

Study by Elias Dominguez- Comesana et al. suggests serum level of PCT to be related to presence of postoperative abdominal infection [10].

Thus comparing our study with other studies we would like to utilise the diagnostic efficacy of procalcitonin and C- reactive protein in detection of bacterial infection in abdominal sepsis. A number of related studies were reported [11-14]. Ramraoet. al. reported on Role of C- Reactive Protein in Acute Appendicitis[15].

CONCLUSION :

PCT and CRP are related to severity of sepsis, with higher concentrations in ongoing infection. Different sensitivity and kinetics shows combination of both PCT and CRP as suitable biomarkers in diagnosing sepsis after infectious etiology.

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