

Original Research Article

Comparative Study between Serum Ischemia Modified Albumin, Nitric Oxide Products and Malondialdehyde in Patients of Sepsis

Sibasish Sahoo¹, Brijesh Mukherjee², Saurav Patra³

¹Senior Resident, Department of Biochemistry, All India Institute of Medical Sciences, Raipur, Chhattisgarh, India.

²Assistant Professor, Department of Biochemistry, Hi-tech Medical College & Hospital(Rourkela) India.

³Associate Professor, Department of Biochemistry, KIMS (Bhubaneswar) India.

Corresponding Author: Sibasish Sahoo

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ABSTRACT

Background: Approximately 3,000 patients die of severe sepsis every day. In the acute phase, the clinical symptoms are nonspecific and it is often underappreciated in clinical practice. There is delayed diagnosis due to shortcomings in both culture and available blood tests.

Materials and methods: A cross sectional (case control) study was carried out with two groups depending on the features of systemic inflammatory response syndrome and diagnosed cases of septicemia. We tried to compare serum Ischemia Modified Albumin, nitric oxide and malondialdehyde with serum CRP in patients with systemic inflammatory response syndrome and septic patients admitted in ICU. These parameters were also compared with physiological parameters like Pulse Rate, Temperature and Total Leucocyte Counts.

Result: The biochemical marker like Serum IMA, NO, MDA & CRP show the very significant p value when compared between Control Group with patients with systemic inflammatory response syndrome and with septic patients admitted in ICU.

Conclusions: Serum Ischemia Modified Albumin, Malondialdehyde and Nitric Oxide showed a positive correlation with serum CRP which is a established marker of sepsis in total patient group.

Keywords: Ischemia Modified Albumin (IMA), C-Reactive Protein (CRP), NO (Nitric oxide), MDA (Malondialdehyde), Systemic Inflammatory Response Syndrome (SIRS).

INTRODUCTION

Sepsis is a syndrome that is defined as a systemic inflammatory response to an infection that has a proven or suspected microbial etiology. [1] It is a life-threatening medical condition characterized by an overwhelming infection in the presence of infective agents or its toxins in the bloodstream. [2]

Sepsis is not a single disease entity but a progressive disorder. If the bacteria in the blood do not produce any symptoms, the condition is called bacteremia, whereas bacteremia manifesting symptoms in severe forms

leads to sepsis. The bacterial infection invariably is characterized by hyperthermia or hypothermia, tachypnea, tachycardia and leucocytosis or leucopenia. [3] There is a potential risk to life as it increases the risk of mortality, when mild form culminate in severe form of sepsis, invariably there is progression to multi organ failure which ultimately leads to death. [4]

Sepsis is among the most common reasons for admission to intensive care units (ICUs) throughout the world. [5] It is associated with high mortality, morbidity, and leading to high cost of treatment.

Severe sepsis affects approximately 7.51 lacs patients world-wide per annum. Mortality from severe sepsis and septic shock approaches 30 - 70 % with 2.15 lacs deaths annually. [6,7] During the last decade, incidence of sepsis in the United States has tripled, making it 10th leading cause of death. In the United States alone, approximately 7.50 lacs cases of sepsis occur each year, approximate of which 2.25 lacs are fatal. [8]

According to a nationwide study, one out of four patients in intensive care units suffers from sepsis. In all ICU admissions, statistics reveals that 5% to 20% patients suffer from severe form of sepsis and is the leading cause of death in non-coronary ICU. 25-35% of patients with severe sepsis and 40-55% of patients with septic shock die every day. [9] Approximately 3,000 patients die of severe sepsis every day in India. [10]

Its rising incidence, new etiologies, and appearance in new populations of patients have been attributed to changing demographics and the increased use of more potent broad-spectrum antibiotics, immunosuppressive agents, and invasive technology in the treatment of inflammatory, infectious, and neoplastic diseases.

Clinically identifying patients with sepsis and in particular septic shock is a definite challenge to the clinician. A variety of clinical and laboratory findings are helpful, but there is no single test to identify or assess the severity of sepsis. As the menace of sepsis increases there has been a steady increase in number of various research works in fields concerning the prevention, assessing various risk factors, treatment modalities, and outcome of septicemia. Biochemical markers like Procalcitonin, C Reactive Protein, Ferritin, Lactoferrin, Neopterin, Serum Amyloid A, are useful in early diagnosis of sepsis. [11] But unfortunately most of these parameters are costly and not available in all laboratories except for few highly advanced ones in metropolis. Hence

there is a need to find out alternative methods for early diagnosis and onset of sepsis at a lesser cost.

A modification of human serum albumin (HSA) caused by ischemia has been recently proposed as a serum biomarker of myocardial ischemia. Under physiological condition, the amino terminal end (N-terminal) of HSA binds transitional metals such as cobalt, copper and nickel. During ischemia, several changes occur in the amino acids terminal end (N-terminus) of HSA, possibly caused by oxidative free radical, which reduces its capacity to bind transition metals, notably cobalt. This new, chemically changed albumin is called Ischemia Modified Albumin (IMA). [12,13] IMA a bio-marker for the early detection of myocardial ischemia in acute coronary syndromes. [14] Several lines of evidence suggest that IMA is elevated in various non cardiac pathologies where hypoxia and oxidative stress are found. [15]

Nitric oxide (NO) is responsible for the hypotension and cardiovascular collapse in septic shock. Therefore, a lot of medical research is focused on combating NO, which is also a messenger molecule in the body. Attempts to inhibit its production paradoxically led to a worsening of the organ damage and in an increased lethality in a clinical trial in sepsis patients. This led to the assumption that NO also has positive effects in sepsis, but up to now NO remained a prime suspect for the pathogenesis of shock. [16]

Reactive oxygen species degrade polyunsaturated lipids, forming malondialdehyde. [17] This compound is a reactive aldehyde and is one of the many reactive electrophile species that cause toxic stress in cells and form covalent protein adducts referred to as advanced lipoxidation end-products(ALE), in analogy to advanced glycation end-products (AGE). [18] The production of this aldehyde is used as a biomarker to measure the level of oxidative stress in an organism. [19]

Now, there is a search for bio-marker with high sensitivity and specificity for the diagnosing sepsis and assessing its progress to severity. Keeping this in view the study was done to evaluate the role and performance of Ischemia Modified Albumin (IMA), Malondialdehyde (MDA) and Nitric oxide (NO) in early diagnosis and severity assessment of sepsis with an aim to elucidate their beneficial role as specific and cost effective biochemical markers for monitoring and treating sepsis.

MATERIALS AND METHODS

The present study was carried out in the department of Biochemistry, along with the collaboration of Intensive Care Unit under Department of Anaesthesia of Kalinga Institute of Medical Sciences (KIMS), Bhubaneswar from November 2011 to January 2013.

Patients admitted to the ICU were taken as cases. Blood was collected in clean sterile vials before the treatment was started. Consent was obtained from all subjects.

Ethical committee approval was obtained from college's Ethics Committee:

The study includes 3 groups.

GROUP I - 90 healthy volunteers.

GROUP II - 31 patients with systematic inflammatory response syndrome (SIRS) in ICU.

GROUP III - 45 septicemia diagnosed patient from ICU.

The details of the patient's clinical data which include the time of presentation at the emergency department were entered in a specialized Proforma made for the purpose of the study.

Exclusion Criteria for Sepsis Subjects:

- Age <18 and >60
- Chest pain with ST elevation myocardial infarction or dynamic ST changes on ECG
- Pregnant women
- Drug abuse
- Immunosuppressive therapy
- Severe Liver disease

- Severe hypoalbuminemia

METHODOLOGY

Routine biochemical parameters include:

Fasting blood glucose

Serum urea

Serum creatinine

Total protein

Serum albumin

Liver function test

Serum CRP

Special parameters are:

Serum Ischemia Modified Albumin (IMA)

Serum Malondialdehyde (MDA)

Serum nitric oxide (NO)

All the analysis was estimated by Autoanalyzer

Sample Collection: After obtaining informed consent of the patient, blood samples were collected for routine and specific tests.

Collection of blood Sample: 5 ml of blood was collected from all enrolled patients who were not given therapy for septicemia for assessment of IMA, MDA and NO products. Biochemical parameters were evaluated after separation of the serum.

A detailed physical examination of the patients were carried out such as height, weight, body built, pallor, icterus, cyanosis, thyroid gland, edema, lymph node enlargement, temperature, pulse, blood pressure, systemic examination such as CVS, CNS and Respiratory Examination.

The study designed for this thesis was framed accordingly, comprising of 90 controls and 76 cases. 31 cases were categorized as Group I, i.e. patients admitted with signs of SIRS. These patients showed abnormal parameters like Temperature, Heart Rate and Respiratory Rate and a pathologically fluctuating Total Leucocytes Count. 45 cases categorized as Group II were clinically diagnosed sepsis.

Estimation of Serum Ischemia Modified Albumin Level: (BAR OR ET AL 2000)

IMA is measured by an indirect method based on the albumin cobalt binding (ACB) colorimetric assay. Serum IMA

was measured by addition of a known amount of Co^{2+} ($\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$, 1g/l, sigma) to serum specimen and further assessment of the unbound Co^{2+} by colorimetric assay using dithiothreitol (DTT, 3g/l, sigma) for colour development, as previously described by Bar-Or et al. [20]

Principle: Human serum albumin has an inherent property of binding with metals like cobalt & nickel etc at its N-terminal region. But during ischemia, the N-terminal portion of albumin is affected due to acetylation /depletion of one or more amino acids & result in ischemia modified albumin (IMA). Ischemia modified albumin loses its ability to bind cobalt and other metals.

Cobalt happens to be an indicator in this assay. [21] Here known amount of cobalt is added to serum sample & the unbound cobalt is measured by the intensity of coloured complex formed after reacting with dithiothreitol by spectrophotometer.

Estimation of Nitric Oxide:

Estimation of nitrite by Griess Method:

Since nitric oxide has a half life of 1 to 3 seconds in the blood it is very difficult to measure it directly. Nitric oxide gets converted to Nitrate and nitrite in blood which is its end product. So estimating the nitrate and nitrite level in blood will give indirectly the level of nitric oxide produced in the blood.

Principle: In acid solution nitrite is converted to nitrous acid (HNO_2) which diazotizes (N=N-) sulphanilamide. This sulfanilamide diazonium salt then reacts with N-1-naphthyl ethylenediamine dihydrochloride to produce a chromophore i.e. is a stable azo compound which is measured at 540nm. [22]

Estimation of Serum Malondialdehyde Level: (Sato K, 1978) (As Thiobarbituric Acid Reactive Substances)

Principle: Polyunsaturated fatty acids react with molecular oxygen to undergo free radical mediated auto-oxidation. Numerous peroxides and aldehyde

compounds are formed during the process. The non-volatile primary peroxidation products decompose to form malondialdehyde during the acid heating stage in the laboratory. The 3- carbon compound MDA forms a characteristic chromogenic adduct with 2 molecules of thiobarbituric acid. This has maximum absorbance at 532 nm, which can be detected by spectrophotometer. Anhydrous Na_2SO_4 was added to avoid interference by bilirubin. [23]

All above tests were standardized in the departmental laboratory. Biochemical test like Fasting blood glucose, Serum urea, Serum creatinine, Total protein, Serum albumin, Liver function test & Serum CRP were also estimated by reagent kit method.

Statistical analysis: Results are presented as Mean \pm SD. Statistical significance and difference from control and test values were evaluated by Z-test and F-Test was used for comparison of variance. Student's unpaired t-test was not applied due to large sample size. It is evident from various opinions of eminent statisticians that t-test should be applied to calculate p value when the sample size is less than 30. Z test is more accurate when the study is done on a large sample size. P-value of $P < 0.01$ and $P < 0.05$ were considered significant. Correlation coefficient was used to describe the effects of independent and dependent variables by Pearson correlation test. All statistical analyses were done using Microsoft Excel for Windows VII version, SPSS (Statistical Package for Social Sciences) and GraphPad Prism 6.0 version.

RESULTS & DISCUSSION

Sepsis is characterized as the combination of pathologic infection and physiological changes known collectively as the systemic inflammatory response syndrome (Martin, 2003). [24] This response results in physiological alterations that occur at the capillary endothelial level. In the early stages, the

clinical manifestations of this process are nonspecific and it is often underappreciated in clinical practices. However, early recognition of this syndrome is vital in reducing mortality in sepsis. From clinical studies sepsis can be seen as a continuum of severity that begins with an infection, followed in some cases by sepsis, severe sepsis - with organ dysfunction - and septic shock. There has been a substantial increase in the incidence of sepsis during the last decades, and it appears to be rising over time, with an increasing number of deaths (Bone, 1992).^[25] Advanced age, underlying co morbidities and number of organ dysfunction are factors which are consistently associated with higher mortality in severe sepsis and septic shock. However, the incidence of severe sepsis in this last study could have been overstated due to the factor that authors used ICD-9-CM coding for the identification of the syndromes. The prevalence of severe sepsis and septic shock in patients admitted to intensive care units is 11-30% and 6-10%, respectively. Studies using data from admissions to emergency departments and intensive care units have also found increasing rates of severe sepsis and septic shock in the last decades.

C-Reactive Protein: A significant difference ($p < 0.05$) was seen between the mean values of the control group (0.28 ± 0.09) and cases (11.08 ± 10.69). The Mean \pm SD values in group I and II 0.92 ± 0.37 mg/dl and 18.09 ± 8.48 are respectively. There was no significant difference when control group was compared with group I ($p < 0.08$) but the difference was significant when compared between control group and group II ($p < 0.0001$). There was also significant increase in serum CRP values when compared between group I and group II ($p < 0.04$). The above findings show that serum C Reactive Protein does not increase significantly in sepsis at early stage but increases rapidly with onset

of symptoms of infection. Nora Hofer et al concluded in their study that CRP was most widely available, most studied and most used laboratory tests for neonatal bacterial infection and despite the continuing emergence of new infection markers it still plays a central role in the diagnosis of early onset sepsis of the neonates.^[26] CRP has the advantage of being well characterized in numerous studies and was found to be the best marker to diagnose sepsis in neonates.^[27] Pova P et al also described that CRP is useful in detection of sepsis and it is more sensitive than currently used markers such as BT and WBC.^[28]

Ischemia modified albumin: The mean \pm SD value of IMA in control group was 45 ± 6.39 U/ml and in the cases it was 92.52 ± 21.85 U/ml. There was a significant difference ($p < 0.0001$) between both these groups. The results in group I and II are 71.61 ± 9.58 U/ml and 106 ± 15.21 U/ml respectively. The mean were higher and the difference were significant ($p < 0.0001$) to that of the control value. There was also significant increase ($p < 0.0001$) in serum IMA values when compared between group I and group II. Serum IMA is an established inflammatory marker of sepsis as demonstrated by the studies done by N-Komitopoulous et al^[29] and Said Sami Erdem et al,^[30] concluding that Serum IMA may be useful as prognostic biomarker as it correlates with severity of sepsis.

Malondialdehyde: A significant ($p < 0.0001$) increase was seen between the mean \pm SD values in the controls (0.91 ± 0.39) and cases (4.49 ± 1.19). The Mean \pm SD values in group I and II are 2.68 ± 1.34 nmol/L and 5.76 ± 1.26 nmol/L respectively. All these values are significantly higher than the control value. There was also significant increase in serum malondialdehyde values when compared between group I and group II ($p < 0.0001$). Serum Malondialdehyde

represent a state of unbalanced oxidative stress when exposed to free radicals injury by two mechanisms - activated phagocytes and reperfusion as stated by the studies done by Leonardo Lorente et al [31] and Irfan Altuntas et al [32] which demonstrate that serum malondialdehyde measure the degree of oxidative cellular pathology in the cellular level and can be used as a prognostic marker of sepsis.

Nitric Oxide Products: The mean and SD value in control group was 13.69 ± 3.37 $\mu\text{mol/L}$ and in the cases it was 44.10 ± 16.09 $\mu\text{mol/L}$. There was a significance difference in the mean values ($p < 0.0001$). The Mean \pm SD values in group I and II are 29.26 ± 6.67 $\mu\text{mol/L}$ and 54.33 ± 12.20 $\mu\text{mol/L}$ respectively. All these values are significantly higher than the control value. There was also significant increase in serum nitric oxide products (nitrites and nitrates) values when compared between group I and group II ($p < 0.0001$). Serum nitric oxide is oxidative stress marker. Patients with high serum nitric oxide level are at a significant higher risk of sepsis and mortality as highlighted in the studies of Mettu-SR et al [33] and Barthlen W et al. [33] Study of Evan et al [34] also suggest that serum nitric oxide may be responsible for the hypotension seen in septic shock. All these studies demonstrated that raised serum nitric oxide is marker of oxidative stress in the body and its elevated level is related to bad prognosis.

Pearson Coefficient Of Correlation Of Biochemical Markers: In Group I, there was significant correlation between serum CRP and serum IMA ($r = 0.48, p < 0.0001$) and serum CRP and serum NO ($r = 0.50, p = 0.004$) but correlation between serum CRP and serum MDA was moderate ($r = 0.41, p = 0.02$). The correlation between serum IMA and MDA ($r = 0.53, p = 0.002$), serum IMA and NO ($r = 0.69, p = 0.0001$) and MDA and NO ($r = 0.49, p = 0.005$). As already discussed

patients in this group have raised serum CRP, serum IMA, serum MDA and serum NO levels when compared to controls.

In Group II, a significant correlation was seen between all the parameters i.e. between serum CRP and serum IMA ($r = 0.56, p < 0.0001$), serum CRP and serum MDA ($r = 0.53, p = 0.0001$), serum CRP and serum NO ($r = 0.48, p = 0.0001$), serum IMA and serum MDA ($r = 0.73, p = 0.0001$) serum IMA and serum NO ($r = 0.76, p = 0.0001$) and between serum MDA and serum NO ($r = 0.66, p = 0.0001$).

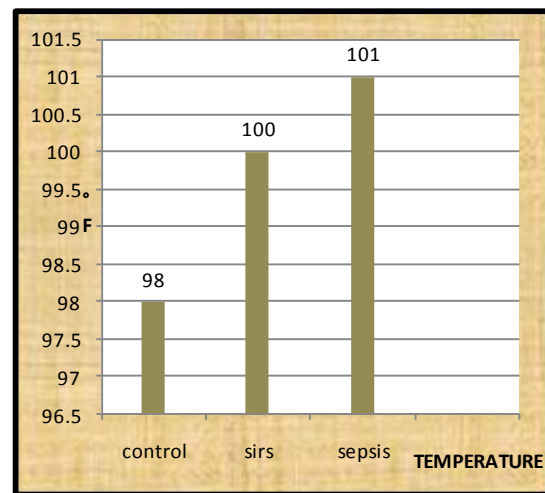


FIGURE- 1: Mean of Temperature in Fahrenheit in different groups.

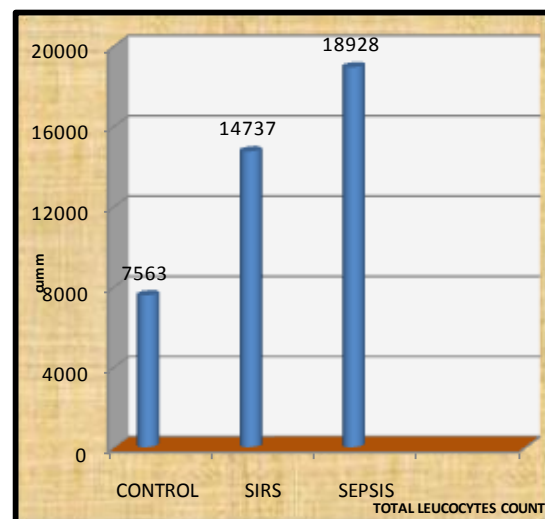


FIGURE- 2: Mean of Total Leucocytes Count in different groups.

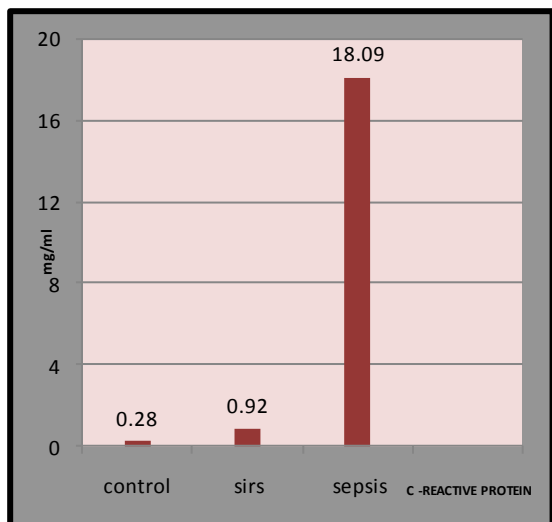


FIGURE- 3: Mean of Serum C Reactive Protein in different study groups.

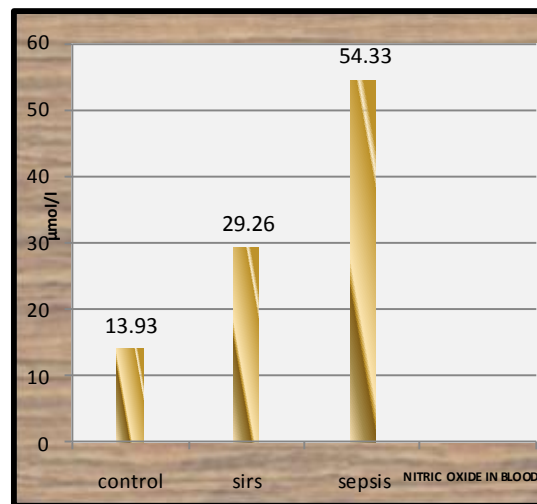


FIGURE-6: Mean of Serum Nitric Oxide in different study groups.

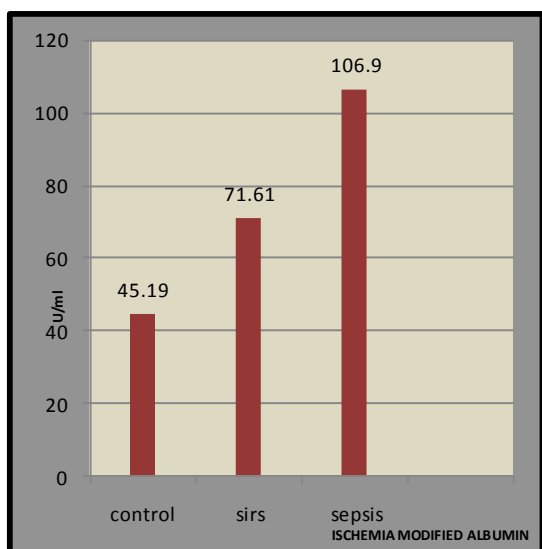
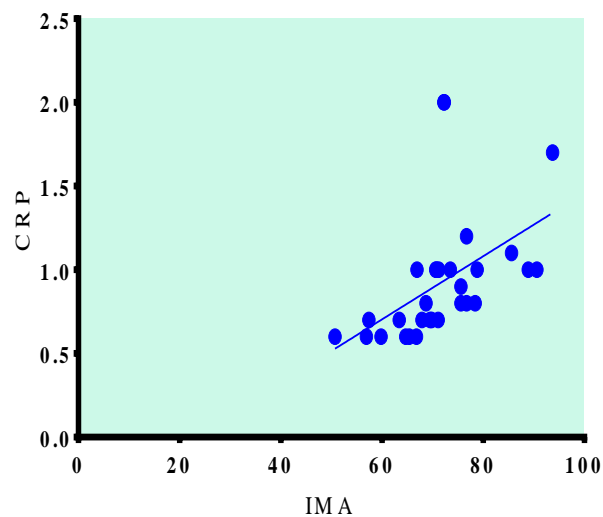


FIGURE-4: Mean of Serum Ischemia Modified Albumin in different study groups.

CORRELATION (IMA & CRP IN GROUP I)



CORRELATION (IMA & MDA IN GROUP I)

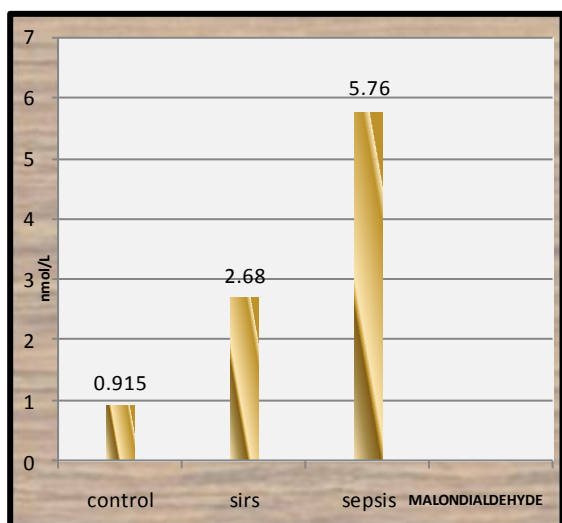
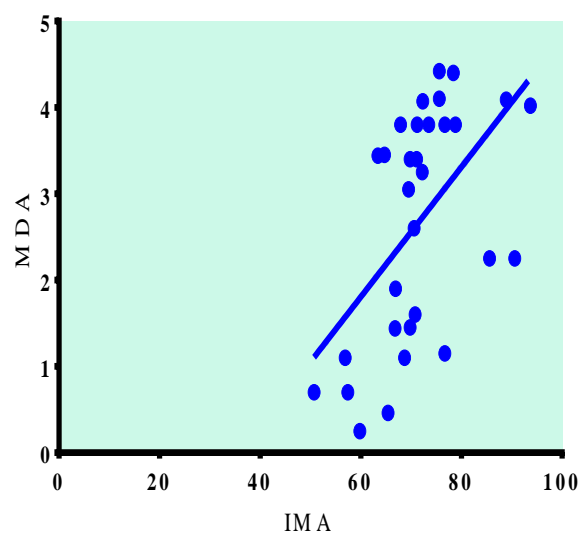


FIGURE-5: Mean of Serum Malondialdehyde in different study groups.

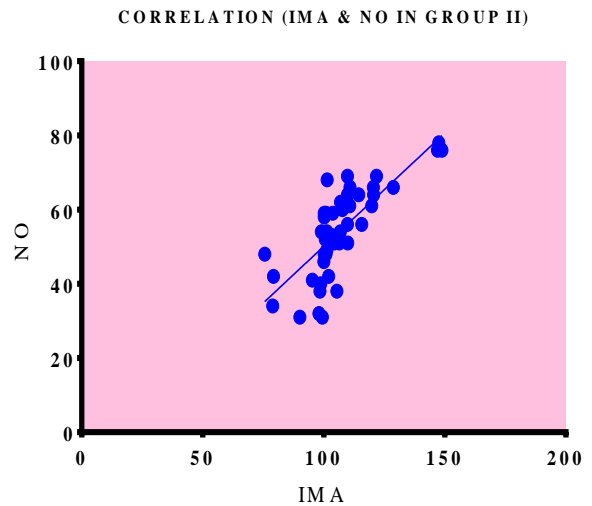
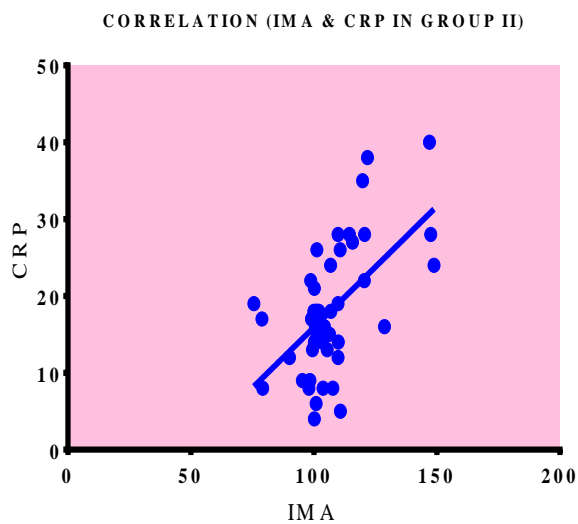
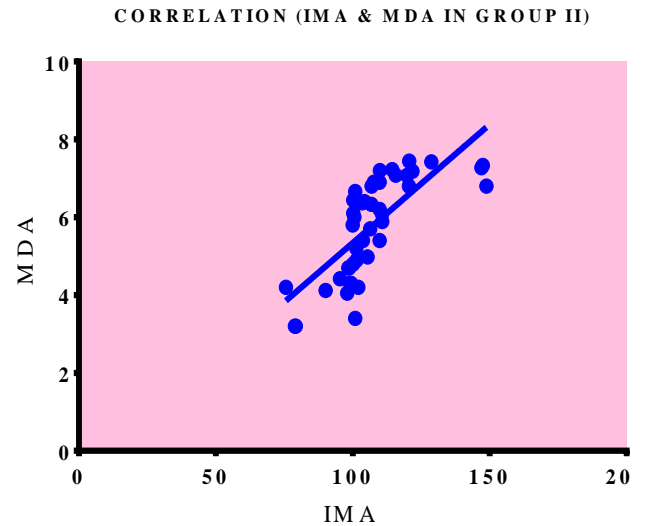
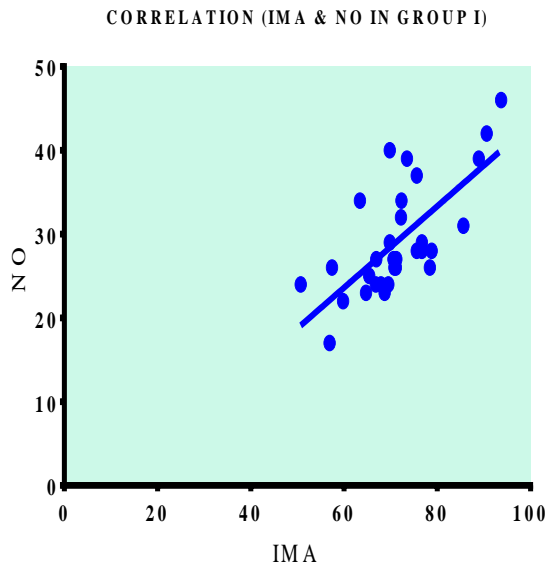


Table No- 1: Biochemical Markers Of The Study Group

BIOCHEMICAL PARAMETERS	CONTROL(n=90)	GROUP I(n=31)	GROUP II(n=45)
CRP	0.28 ± 0.09	0.92 ± 0.37	18.09 ± 8.48
IMA	45.19 ± 6.39	71.61 ± 9.58	106.90 ± 15.21
NO	13.69 ± 3.37	29.26 ± 6.67	54.33 ± 12.20
MDA	0.91 ± 0.39	2.68 ± 1.34	5.76 ± 1.26

Table No-2: Comparison Of Variable By Applying Z Test

Parameter		Group A Control Vs Case	Group B Control Vs SIRS	Group C Control Vs Sepsis	Group D SIRS Vs Sepsis
IMA	Z	7.40	4.13	9.65	3.68
	P	0.0001**	0.0001**	0.0001**	0.0002**
NO	Z	9.02	4.62	12.05	3.75
	P	0.0001**	0.0001**	0.0001**	0.0002**
MDA	Z	9.07	4.42	12.29	2.23
	P	0.0001**	0.0001**	0.0001**	0.01**
CRP	Z	120	-1.7	197.88	-2.04
	P	0.0001**	0.08	0.0001**	0.04*
TEMP	Z	-2.02	-1.25	-2.50	-0.833
	P	0.04*	0.21	0.012**	0.404
TLC	Z	7.54	5.60	8.88	1.62
	P	0.0001*	0.0001**	0.0001**	0.10
PR	Z	4.74	2.59	6.77	0.86
	P	0.0001**	0.0096**	0.0001**	0.38
RR	z	1.17	1.71	0.821	-0.50
	p	0.24	0.08	0.41	0.61

Significant*, Highly significant**

Table No-3. Correlation Coefficient Of Biochemical Markers Of: Group I (Sirs)

BIOCHEMICAL PARAMETERS	CORRELATION COEFFICIENT	CRP	IMA	MDA	NO
CRP	Pearson Correlation	1			
	Sig. (2-tailed)				
	N	31			
IMA	Pearson Correlation	0.488	1		
	Sig. (2-tailed)	0.005			
	N	31	31		
MDA	Pearson Correlation	0.418	0.538	1	
	Sig. (2-tailed)	0.02	0.002		
	N	31	31		
NO	Pearson Correlation	0.503	0.699	0.492	1
	Sig. (2-tailed)	.004	0.0001	.005	
	N	31	31	31	31

Table No-4: Correlation Coefficient Of Biochemical Markers Of Group II (Sepsis)

BIOCHEMICAL PARAMETERS	CORRELATION COEFFICIENT	CRP	IMA	MDA	NO
CRP	Pearson Correlation	1			
	Sig. (2-tailed)				
	N	45			
IMA	Pearson Correlation	0.565	1		
	Sig. (2-tailed)	0.0001			
	N	45	45		
MDA	Pearson Correlation	0.531	0.737	1	
	Sig. (2-tailed)	0.0001	0.0001		
	N	45	45	45	
NO	Pearson Correlation	0.485	0.761	0.667	1
	Sig. (2-tailed)	0.001	0.0001	0.0001	
	N	45	45	45	45

Table No-1: Describe serum CRP, IMA, NO and MDA in three groups i.e; control Group, Group I and Group II. The mean of the above biochemical markers of the Study Groups i.e; Serum CRP, IMA, Nitrates and MDA were increased in group I when compared with the control Group and increased maximum with Group II when compared with Group I and the Control Group.

Table No-2: Shows the significant z value and p value of the biochemicals and general physical parameters of sepsis. The p value were highly significant in all the four groups for Serum IMA, NO & MDA. General parameters like Temperature, Total Leucocyte Count, Pulse rate and Respiratory rate were not significant when compared between the Group I(SIRS) and Group II(SEPSIS). More ever Temperature and Serum CRP was also not significant when compared between the Control Group and the Group I. Respiratory Rate were not significant in any of the Groups.

CONCLUSIONS

An ideal marker for diagnosis of sepsis would be specific for the systemic

inflammation resulting from infection. As most cases of sepsis are associated with bacterial and fungal infection, blood culture is often considered the gold standard for diagnosis of infection. However, it lacks specificity and sensitivity. Nevertheless, current guidelines recommend culture for all the patients suspected of having sepsis, with the caveat that more than 50% of culture may be negative in the patients who have severe sepsis or septic shock. In addition, there is a substantial time delay of at least 24 hours for a positive culture report and 5 days for a negative culture report. This delay hinders the clinician's ability to make informed treatment decision in a situation that requires immediate action.

In the acute phase, the role of the clinical microbiology laboratory is usually marginal, as clinicians are aware that at least 24 to 72 hrs are necessary for the confirmation of an infectious etiology, identification of the pathogen, and evaluation of its antimicrobial susceptibility. The role of blood cultures is crucial for the correct fine-tuning of antibiotic therapy. However, several factors such as empirical antibiotic therapy

initiated before blood sampling or the presence of fastidious pathogens may have a negative impact on the diagnostic yield of blood cultures even when a bloodstream infection is strongly suspected.

Traditional markers of systemic inflammation such as C-reactive protein and WBC count also have proven to be of limited utility in identifying ill patients who require antimicrobial therapy. The sensitivity and specificity of these measurements for bacterial infections are low.

These shortcomings in both culture and available blood tests have driven researchers to find other more specific markers. So this study was conducted to find out a suitable endogenous marker which can detect sepsis and predict its severity. A cross sectional (case control) study was carried out with 76 cases divided into two groups depending on the features of systemic inflammatory response syndrome and diagnosed cases of sepsis. We tried to evaluate the Ischemia Modified Albumin, Malondialdehyde, and the Nitric Oxide levels in septic patients and compare it with age matched normal subjects. The various findings were tabulated and analyzed to arrive at appropriate conclusion. SIRS and Septic patients when compared to controls showed higher Temperature, Respiratory rate, Heart rate and Total leucocytes Count. In our study comprising of 76 cases and 90 control subjects there was significant raised levels of Ischemia Modified Albumin, Malondialdehyde and Nitric oxide in the patient group compared to control group.

Even though C Reactive Protein increases in inflammation, in this study, it was found that the C Reactive Protein level between control group and SIRS was not significantly different but the levels of C Reactive Protein was significantly raised in sepsis group.

The level of Ischemia Modified Albumin, which is an established marker

of ischemia, was found to be significantly raised in both SIRS and sepsis patients, with a greater rise seen in sepsis.

Ischemia Modified albumin also assesses the severity of sepsis when correlated with APACHE II scoring methods which is preferably used by the physician and anesthetists to diagnose sepsis and its severity clinically.

The levels of Malondialdehyde, a marker of oxidative stress was significantly higher in patients compared to controls suggesting increased oxidative stress in septic patients.

Nitric Oxide levels showed significant higher levels in the patient group compared to control group, indicative of a major role of nitric oxide as a vasodilator in sepsis.

Serum Ischemia Modified Albumin, Malondialdehyde and Nitric Oxide showed a positive correlation in total patient group. Between SIRS and Septic patients there were significant differences in these three parameters.

In this study Serum C-Reactive Protein had positive correlation to Serum Ischemia Modified Albumin, Malondialdehyde and Nitric Oxide levels in total patient group.

The study design of this thesis was cross sectional comprising of a small group of patients. The findings of this study are only suggestive. A longitudinal study with larger patient group can be done to arrive at definite conclusion.

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