# Assessment of diagnostic validity of Procalcitonin in burns sepsis patients – A prospective study


**A dissertation submitted to the Tamil Nadu Dr M.G.R Medical University in partial fulfillment of the requirement of the award Of M.Ch. Branch III (Plastic Surgery) degree August 2010-2013**

# CERTIFICATE

I hereby declare that this dissertation entitled **"Assessment of diagnostic validity of Procalcitonin in burns sepsis patients – A prospective study"** is a bonafide research work carried out by Dr. Naveen Kumar H R in partial fulfillment of the requirement for the degree of M.Ch. in Plastic Surgery.

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# ENDORSEMENT BY THE H.O.D. OF PLASTIC SURGERY

This is to certify that this dissertation entitled **"Assessment of diagnostic validity of Procalcitonin in burns sepsis patients – A prospective study"** is a bonafide and genuine research work carried out by **Dr. Naveen Kumar H R** under the guidance of **Dr. Kingsly Paul M** M.S, MCh, Professor and unit head, Department of Plastic Surgery, Christian Medical College, Vellore.

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# INDEX

# ABSTRACT


TITLE OF THE ABSTRACT : To asses the Diagnostic validity of Procacitonin in Burns Sepsis patients.

DEPARTMENT :Plastic and Reconstructive surgery
NAME OF THE CANDIDATE :Dr. Naveen Kumar H R
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AIM / OBJECTIVE:

To asses the Diagnostic validity of Procacitonin in Burns Sepsis patients.

MATERIAL AND METHODS:

This was a prospective diagnostic study done for a period of 9 months involving 36 cases who sustained > 20% TBSA of second degree burns. The criteria explained by the American Burn Association (ABA – 2007) were used as the reference standard to diagnose sepsis. Patients were continuously monitored for the development of signs and symptoms of sepsis. Procalcitonin (PCT) estimation was done at the time of sepsis and without sepsis. The values of PCT correlate with the sepsis parameters of American Burn Association. Data was analysed using Receiver operating curve analysis, Fisher exact test, t test, Mann whitney U test.

RESULTS:

The predictive ability of the PCT was determined by using the ROC (Receiver operating curve) and the area under the curve was calculated with 95% confidence intervals. Analysis of the coordinate points reveled the best threshold values of PCT for the prediction of sepsis based on the combination of sensitivity and specificity of each proposed threshold. The cut off value was 5ng/ml based on the ROC analysis at the sensitivity of 88.9% and specificity of 83.3% with area under the curve was 91%.

CONCLUSION:

Procalcitonin has sensitivity of 88.9% and specificity of 83.3% in diagnosing sepsis in burns patients at the cut off value of 5 ng/ml..

# Introduction

## Introduction:

Sepsis is one of the major cause of mortality in burns patients.[1] Sepsis is defined as systemic inflammatory response with documented infection. If not treated, then the infection will lead to organ dysfunction, hypoperfusion and hypotension called as severe sepsis. Later it will end up with septic shock. Systemic inflammatory response syndrome (SIRS) can be due to either infectious or non infectious cause. In major trauma and burns patients it is always difficult to differentiate whether SIRS is a result of injury itself or due to superimposed infection. Most of the clinical signs of infection such as fever, tachycardia , leucocytosis were also present in SIRS.

Thus to overcome this a consensus panel was formed by American burns association and guidelines were framed to define sepsis in burns patient. In this the definition of SIRS and severe sepsis was excluded and the range of vital parameters were raised, platelet count and patient glucose level included. Inability to feed the patient enterally for more than 24 hrs was also one of the criteria. To diagnose it as sepsis, infection should be documented or the infection should respond to the antibiotic started empirically. These guidelines were based on the consensus and not on any prospective clinical studies.

Clinically it is very important to identify systemic infection at the earliest of its stage to initiate antibiotic therapy and to prevent further mortality.[2] Though blood culture is the gold standard to diagnose systemic infection it will take several days to get the growth of infecting organism and also the presence of negative culture doesn't assure the absence of infection. So it is necessary to identify the indirect circulating markers of systemic infection that can be rapidly assessed and reliable. So many markers have been

explained in the literature eg., CRP – C reactive protein, TNF □ , IL-6 etc. But Cytokine and non cytokine markers are not used routinely in burned patients. The marker that have been consistently elevated in patients with infection is procalcitonin(PCT). Studies have shown that increased plasma levels of PCT are sensitive and specific marker of infection.[3]

The marker is more specific for the bacterial infection and increase several folds within 4 hrs of infection, reaches peak by 6 hrs and plateau by 8-24hrs, then return to baseline by 2-3 days. Its half life is 24-30hrs. These qualities of the marker made it clinically suitable and to repeat at regular intervals.

In the past many studies had been done to assess the PCT value both in burns and non burns cases. Due to the localized infection the value of PCT may be raised marginally even in the absence of sepsis. So the cut off value considered in the previous studies has very low threshold for the diagnosis of sepsis. This study done to assess the PCT value in burns patients and also to find a cut off value to suspect sepsis at initial stages and include it as a protocol in our set up.

# Aims & objectives

**Aims and objective:**

1) To find the diagnostic validity (sensitivity and specificity) of procalcitonin in burns sepsis patients.
2) To find a cut off value of procalcitonin to diagnose sepsis in burns patients.

# Materials & Methods

## Materials and methods :

This is a prospective study done for a period of 9 months from March 1st , 2012 to November 31st , 2012 in the Department of Plastic Surgery, Christian Medical College and Hospital, Vellore. This study was approved by the Institutional Review Board. There were 36 patients involved in this study.

Inclusion criteria : All patients with more than or equal to 20% burns.

Exclusion criteria : All patients with less than 20% burns.

All patients presented with 20% or more of burns admitted in the burns ward of CMC Hospital were included in the study. If the patient got admitted within 24 hr of injury the resuscitation protocol of our burns unit was started which involves

- Admission to the burns unit.
- Insert a central line preferably in non burnt areas.
- To place a Foleys catheter to measure urine output.
- To start fluid (Ringer lactate) as per parkland formula.
- Burn wound care and silver sulfadiazine dressing.
- Insert naso gastric tube in major burns
- I.V. morphine as analgesic round the clock.
- To send all base line blood investigations.

  (Hemoglobin, Total and differential count, Random blood sugar, Creatinine, electrolytes).

On the first day of resuscitation period we maintained a urine output of 30-50ml/kg/hr. we titrated the fluid based on urine output. On second day of resuscitation colloid was started. We infused 0.5ml/kg/%burns of plasma with 5% dextrose to maintain urine output of 1ml/kg/hr. The Patients were monitored continuously. Every $4^{th}$ hourly Temperature, pulse rate and respiratory rate were recorded daily from the day of admission. Patient daily calorie intake was documented. Twice a week baseline blood investigations were done. Pus culture of the wound, blood culture, urine culture and sputum culture were done from third day of burns depending on the patient condition. All the parameters necessary to diagnose burns sepsis according to American Burn Association (ABA) consensus were documented in a Chart to diagnose sepsis (Chart attached in Annexure 1). This was the reference standard of our study.

American burn association consensus definition of sepsis and infection :

3 or more of the following :

1. Temperature >39°C or <36.5°C
2. Progressive tachycardia (> 110/min)
3. Progressive tachypnoea (>25/min)
4. Thrombocytopenia < 1 lac (only applies 3 days after initial resuscitation)
5. Hyperglycemia (in the absence of pre-existing diabetes mellitus)
6. Inability to continue enteral feeding >24 h.

Plus documented infection with one or more of the following:

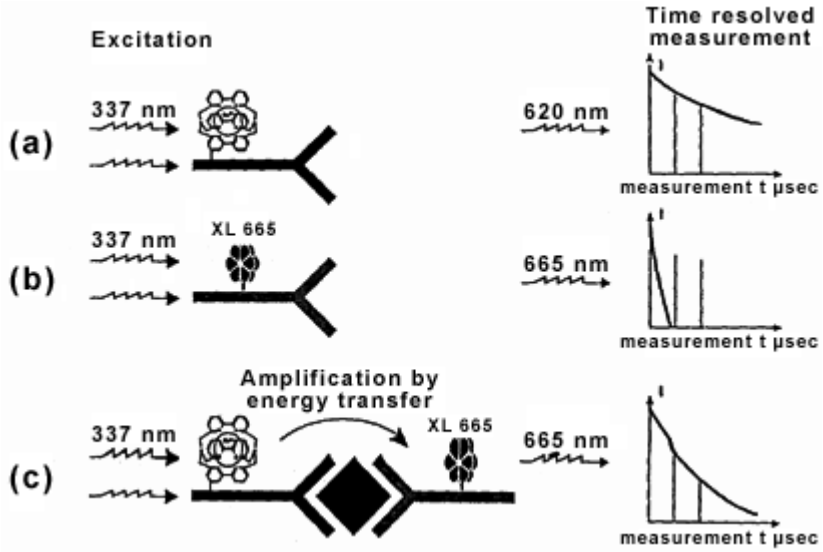
1. Culture positive infection.
2. Pathologic tissue source identified.
3. Clinical response to antimicrobials.

All patients presented with 20% or more of burns were included in the study. The Patients were monitored continuously for any signs and symptoms of sepsis after admission. The sepsis parameter was documented in a Chart daily and this will help the analyser to know exactly at what time period the patient was gone into sepsis. A base line PCT level estimation was done at the time of admission when the patient is not into sepsis. The next PCT level estimation was done when he/she fulfils the criteria of sepsis. So PCT was analysed approximately thrice for each patient, once at the time of admission, sepsis and when patient recovers from sepsis. By doing this each case was served as his/her own control. The collected data was divided into two groups, i.e.: values noted at the time of each pre and post sepsis episode. At the end of the study the data analyser was blind for the collected PCT value. He would be correlating the PCT value with the present sepsis parameter and to assess the diagnostic validity of the test. Those of the patients without an episode of sepsis had a single PCT assay reading at admission which was served as a baseline PCT estimation reading. All the other investigation are being done routinely according to our Burns Protocol. Temperature, Heart rate and Respiratory rate monitoring $4^{th}$ hrly. TC/DC, Platelet count, Random blood sugar - on day of admission and every 3rd day, Wound culture and Blood Culture – on $3^{rd}$ post Burn Day Urine c/s and sputum c/s – depending on the septic foci .Investigation will be repeated frequently depending on the patient condition.

## Procalcitonin estimation:

Procalcitonin measurement in our study was done using the test kits obtained from B.R.A.H.M.S (Kryptor method) Germany. The results were obtained within 19 min of the test. The analytical sensitivity of the test was 0.019ng/ml and the functional assay sensitivity of 0.06ng/ml with a probability of 95%. The Kryptor method consists of sheep polyclonal anti – calcitonin antibody and a monoclonal anti – katacalcin antibody which binds to the calcitonin precursor molecules. The antibodies used in this assay do not show cross reaction with human calcitonin (up to 2.5ng/ml) and katacalcin (up to 10ng/ml) , human a-CGRP and b-CGRP (up to 4 mcg/ml). The interfering substances like icteric , haemolytic, hyperlipemic samples and also samples with turbid or contain fibrin if present then it is signalled by Kryptor.

Measuring principle :



The technology used was TRACE – time resolved amplified cryptate emission (Kryptor – PCT) based on non – radioactive transfer of energy which takes place from europium cryptate to XL 665 and this could only be possible when PCT present in the sample are sandwiched between the antibodies forming Ag-Ab complex. The energy transferred or the intensity of the signal is proportional to the amount of PCT within the sample. These commercially available kits measures both PCT- I , PCT-II and the cleavage products of calcitonin precursor molecule which consists the residues of calcitonin and katacalcin.

# Review of literature

American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) in 1992 described the Systemic inflammatory response syndrome (SIRS) based on clinical and experimental results which is independent of cause.[4]

According to this two or more following criteria should be fulfilled to diagnose as SIRS

1. Temperature > 38 or < 36 degree
2. Heart rate > 90/min.
3. Respiratory rate > 20/min or Paco2 <32mmHg
4. Leucocyte count >12000/<4000/>10% immature (band) forms.

The criteria explained were more sensitive and less specific. In order to improve the specificity there was a meeting regarding this issue in second conference in 2001. Additional criteria were added that defined metabolic, biochemical and functional alterations associated with SIRS. Those criteria were hyperglycemia, edema, elevated plasma C reactive protein, coagulation abnormalities, thrombocytopenia, hyperbilirubinemia and ileus.[5] SIRS can occur in infective and non infective cases. For eg., in burns , multiple trauma, pancreatitis etc. sepsis was defined as SIRS with documented infection.

In 2002 the same consensus also explained the SIRS in children and severe sepsis was defined as sepsis with one of the organ dysfunction like cardiovascular system, ARDS or two or more of other organs dysfunction (respiratory, renal, neurologic, hepatic or hematologic) and Septic shock as Sepsis with arterial hypotension despite adequate fluid resuscitation.

But the extensive wounds in burns patients had chronic exposure to inflammatory mediators which causes fever, tachycardia, tachypnea and resetting of baseline metabolic rate considered as the normal physiologic response. So in order to define sepsis in burns the SIRS category was dropped as this was considered as the protective response of the body towards exaggerated inflammatory condition. Thus in 2007 American Burn Association consensus conference defined sepsis and infection in burns with the following guidelines.[6]

SIRS:

Not applicable in burn patients

Sepsis:

3 or more of the following triggers search for infection

1. Temperature >39°C or <36.5°C
2. Progressive tachycardia (>110 /min)
3. Progressive tachypnoea (> 25/min)
4. Thrombocytopenia (only applies 3 days after initial resuscitation)
5. Hyperglycemia (in the absence of preexisting diabetes mellitus)
6. Inability to continue enteral feeding >24 hrs

Plus documented infection with one or more of the following

1. Culture positive infection
2. Pathologic tissue source identified
3. Clinical response to antimicrobials

Severe sepsis:

Not applicable in burns patients

Septic shock:

Sepsis with persistent hypotension despite adequate fluid resuscitation.

The aim of this guidelines is to have a consistent diagnosis in all burn centres and to help in future research. Still the term SIRS is used to explain the pathogenesis of post burn injury and sepsis. SIRS is also called as hypermetabolic response in burn injury which is more meaningful.

Two hit hypothesis of sepsis :

The pathophysiology of SIRS and sepsis was explained by Two hit hypothesis. The injured host manifest an exaggerated inflammatory response if exposed to secondary inflammatory stimulus during the post injury period. The initial insult resulted in production of lymphokine interferon alpha (IFN$\alpha$) acts as first signal and prime macrophages for increased inflammatory response. A second stimulus causes the primed macrophages to secrete increase amount of TNF $\alpha$. This was not produced in large amount during the initial inflammatory insult. If the primed macrophages were exposed to even small amount of endotoxin at the time of second stimulus then TNF $\alpha$ was produced enormously. T- lymphocytes also become hyper responsive at the post injury period.

Another mechanism of increased responsiveness by macrophages is ligand for Toll like receptors (TLR 2) and TLR 4 following burn injury.[7] These are proteins which forms receptor complexes along with microbial products such as peptidoglycans, lipopolysaccharide and lipoproteins. This theory was also proved by many animal

studies by different authors. When a week old thermally injured sheep exposed to systemic bacterial challenge found increase pulmonary hypertension and hyperdynamic response.[8] Also when combined administration of low dose endotoxin and TNF α in rat model resulted in hypotension and metabolic effects that was seen after giving highly lethal dose of each compound alone.[9]

Inflammatory Mediators of SIRS :

The initial stimulus for the activation and release of inflammatory mediators of SIRS is either major injury or infection. The various mediators were mentioned in brief.

Cytokines: have unique role in causing SIRS after injury. The most important were TNF α, IL 6, IL 1 and interferon (IFNα).

Extensive studies were done on TNF α. This is released by activated macrophages soon after injury.[10] The molecule has its effects both locally and systemically. At the site of burn injury it activates local immune response against antimicrobials and also helps in tissue repair. But systemically it has devastating effects causing tissue injury, organ dysfunction and finally death. The other systemic manifestations of TNFαwere induction of fever, stimulation to secrete acute phase proteins, coagulation cascade activation, myocardial depression, [11] systemic vasodilatation, hypotension, catabolism and hypoglycaemia. The most important effect of TNF α is its ability to induce apoptosis of various cell types that causes tissue injury when present in high concentration in systemic circulation.[12] TNFα also stimulate the release of IL 1 and IL 6.

IL 1 actions are similar to TNF α except it doesn't induce tissue injury or apoptosis by itself instead it potentiates the injurious effects of TNF α.[13]

The function of IL 6 is to induce production of acute phase proteins and acts as growth and differentiation factor for B lymphocytes. It is produced by macrophages, endothelial cells and fibroblasts.

IFNα is the primary cytokine produced at the initial insult by T lymphocytes and NK cells in response to antigen presentation and induction from IL 12 and IL18. The primary functions of IFNα is to amplify inflammatory response of macrophages, induce secretion of inflammatory mediators (TNF α, IL 1) and potentiates the antigen presentation by HLA II complex. The blockade of IFNα markedly decrease the inflammatory effects induced by the bacterial endotoxin.[14]

Chemokines :

The other group of proteins responsible for SIRS is chemokines. Primarily they function as chemotactic factor for leucocytes. Among various chemokines which were described IL 8 is the potent chemoattractant for neutrophils and major factor in recruiting neutrophils to inflammatory foci. IL 8 also mediate tissue injury in lung in response to trauma and burns.[15]

Non cytokine factors : also have role in the pathogenesis of SIRS they were platelet activating factor ( PAF) , Leucotrienes (LT) ,Thromboxane A2.

PAF : This belongs to phospholipid family having a messenger function. It is released by endothelial cells, platelets, neutrophils and regulates the release of cytokines. It also helps in adhesion of neutrophils to endothelial cells. It also causes changes in vascular

permeability and acts as chemotaxis of leukocytes. PAF can trigger inflammation, thrombosis and also mediate molecular and cellular interactions.

Leukotriens (LT) : Synthesized from leucocytes and acts on G- protein coupled receptors. It causes contraction of endothelial cells and encourage capillary leakage thus sustaining the inflammatory response.

(Thromboxane A2)TXA2 : It belongs to eicasanoids family, synthesized from platelets. It promotes platelet aggregation, vasoconstriction and tissue thrombosis.

## Systemic manifestations of the burns patients

This is divided in to early hypovolemic shock phase and delayed phase of systemic inflammation (SIRS) in which monocytes, macrophages and T cells were activated to release various mediators of inflammation mainly cytokines. The activated T cells divided in to Th1 cells secrets proinflammatory cytokines and Th2 cells secrets anti inflammatory cytokines. The cytokines were differentiated from the hormones in a way that these were not secreted by a specialized cells arranged in glandular tissue, it has broad spectrum of activity when compare to hormones and these were either positive or negative regulators of cell cycle, its differentiation, cell survival, apoptosis and transformation.

There are three important factors which determine the effects of SIRS in burns patients:

1. Severity of initial SIRS is proportional to severity of injury.
2. Prolonged SIRS leads to higher complication rate.
3. Adaptive capacity of the host to SIRS.

So lesser the initial insult lesser the SIRS. Prolongation of SIRS can be reduced by adequate fluid resuscitation, excision of necrotic tissue and enteral feeding. The inflammation is mediated by the cytokines which are released in response to mechanical, thermal and ischemia reperfusion injury at the cellular level. The proinflammatory mediators were TNF $\alpha$ and IL- 6. Worsening or prolongation of SIRS were due to inadequate fluid resuscitation, repeated insults by infection, tissue necrosis and endotoxin migration from the intestine. At the same time body responds by producing more anti inflammatory mediators. These were TGF $\beta$ and IL 10. Producing excess of these anti inflammatory mediators will cause immunosupression and patient will exposed to uncontrollable infections.

Till the early 90s the cytokines and acute phase proteins were the markers used to assess the inflammatory response. The rise in the level of these markers is non specific and increase in both infective and non infective foci. The half life of these markers is very low thus making it not suitable for clinical conditions. Also it is not possible to assess the severity of the inflammation and after any therapeutic intervention these markers take longer period to reach the baseline.

To overcome this in 1990s Procalcitonin was first described as infection induced protein detectable in the plasma of patients who present with sepsis.[16] The marker was more specific to the bacterial infections and will not rise if the inflammation was due to viral infection. PCT usually remain low if the infection doesn't lead to inflammatory response.

Induction and synthesis of PCT :

Procalcitonin belongs to CAPA (Calcitonin gene related peptide amylin procalcitonin adrenomedullin) protein family. Calcitonin gene related peptides (CGRP ) I, II and procalcitonin belong to this group. CGRP I and the mRNA of calcitonin precursor were encoded on CALC- I gene on chromosome 11. All these proteins were usually produced in pro – pro form consisting of approximately 100 amino acids to gain access to golgi system. These prtotein has two cysteine residues to form di sulphide bridge and two protein cleavage sites to form final core protein of 35 amino acid which can be amidated.

PCT mRNA is synthesized by CALC- I gene present on chromosome 11 exclusively during inflammation and sepsis. Calcitonin is also product of CALC- I gene secreted from C cells of thyroid gland in normal individuals. PCT producing cells secrete two different types of PCT mRNA responsible for forming PCT – I and PCT – II which has differences at eight C- terminal amino acids. CALC - I gene produce three sequence of proteins and after processing there are nine different proteins. These proteins differ not only with mRNA splicing and procession , but also with respect to their regulation.

The protein secreted depends on the types of cells involved, stimulus for cellular activation and individual susceptibility of various cell types to these stimuli. In C cells of thyroid gland calcitonin produced in the native form and stored in golgi apparatus and released according to the hormonal or metabolic stimulus. In the absence of infection the activity of CALC-I gene is very minimal with negligible PCT I and II levels. Thus the

concentration in the plasma of healthy individuals is 10-50 pg/ml. In humans PCT I and PCT II mRNA is found mainly in liver, lung, kidney and testis.[17] Ex vivo it is possible to produce PCT mRNA in immunocompetent cells like mononuclear cells when it is stimulated by endotoxin.[18]

PCT has secondary and tertiary structure that is modified by post translational processing. Protein modification occurs by glycosylation. Di peptidyl peptidase enzyme located on renal, epithelial and endothelial cells induced by proinflammatory mediators and endotoxin and is responsible for deamidation of PCT.[19] Till now the function of biologically active PCT molecule is not known.

PCT undergo enzymatic cleavage to form N- terminal aminoprocalcitonin fragment (N – pro) and the conjoined calcitonin : katacalcin fragment. These fragments were present in the plasma of septi patients which can be measured. PCT is also synthesized by circulating peripheral monocytes. But this is not the only source. By various studies and animal experiments it is concluded that the liver is responsible for major secretion of PCT at the time of sepsis and infection.[20]

Procalcitonin (PCT) :

Procalcitonin is a peptide precursor of calcitonin hormone which is secreted mainly by the parafollicular C cells of the thyroid gand . Calcitonin is responsible for the calcium metabolism and to maintain the calcium homeostasis in the body. PCT is made of 116 amino acids which is also secreted by the neuro endocrine cells of the liver, lung and intestine only at the time of inflammatory process. The increased PCT at the time of inflammation does not have any role in calcium metabolism.

| **PROCALCITONIN - ng/ml** | |
|---|---|
| Normal | 0.05 |
| Local infection | < 0.5 |
| Systemic infection | 0.5 - 2 |
| Sepsis | 2 – 10 |
| Severe Sepsis | >10 |

The advantage of PCT clinically over other markers is its half life and reactive pattern for an inflammatory stimulus. Its half life is 24h and within 4hr of infection PCT will start increasing and peaks at 6hr, attain a plateau at 8-24hr and then it takes 2-3 days to return to base line. Clinically this will be helpful to repeat the PCT investigation once in 3 days. Regarding other markers like tumor necrosis factor-alpha (TNF-□) having 90 min onset and return to base line in 6h; interleukin-6 (IL-6) onset of 3hr and comes to base line in 8hr and C-reactive protein (CRP) with onset of 12-24 hr with plateau of 20-72 hrs and return to base line by 3-7 days were having less half life when compare to PCT.[21]

**Studies of PCT in sepsis other than Burns**

PCT has been utilised to differentiate bacterial from viral meningitis in children. This will helps in avoiding antibiotics and its adverse effects in meningitis due to viral cause.[22]

PCT is a diagnostic biomarker which can be utilised for the assessment of disease severity and will be the guidance for treating bacterial infections. This diagnostic biomarker will be a complementary for the clinical diagnoses of the infection. So the cut off values will be based on many diagnostic studies. Biomarker should never be utilised alone and always should be considered along with the clinical signs and symptoms of infection.[23]

PCT used as a diagnostic tool for early indicator of sepsis who present to the emergency department. The study was done both in adult and pediatric age group. Empirical antibiotics can be started based on PCT level before the documentation of bacteria and the response can be assessed with serial PCT level measurement.[24,25]

**PCT evaluation related to burns:**

There are studies done in the past related to procalcitonin in burns patient. Most of the studies were done for evaluating the parameters like CRP, ESR and WBC. The changes in these parameters at the time of burns has been compared to the procalcitonin levels and concluded that procalcitonin has higher specificity when the sepsis starts due to bacterial origin. Also it is known that the changes in other markers are not specific as they keep rising in both hypermetabolic response and sepsis. So it is not possible to consider a cut off margin of these markers above which we can consider it as established sepsis.

Normal value of PCT in adult male : 0.05ng/ml. The level of procalcitonin for the diagnosis of sepsis vary in different studies from >0.5 ng/ml to 3ng/ml. Previously one of the criteria for diagnosing burns sepsis was leucocyte count, which may be either leucocytosis or leucopenia. According to the American burn association these counts are very unreliable and thus it has been excluded from the newer definition of burns sepsis.[26]

A Study done by Barati et al regarding Comparison of WBC, ESR, CRP and PCT serum levels in septic and non-septic burn cases concluded that PCT is a highly efficient laboratory parameter involving a simple and rapid bedside test for diagnosis and prognosis of severe infectious complications after burn.[27]

A Study done by Athina Lavrentieva et al , evaluated serum PCT, CRP, leukocyte count and temperature as markers of sepsis and divided the cases in to two groups as sepsis with SIRS and sepsis without SIRS and concluded that PCT is a better marker of sepsis than other inflammatory markers and the area under ROC curve has an acceptable accuracy.[28]

Another study done by D. von Heimburg et al Procalcitonin - a sepsis parameter in severe burn injuries, they assessed the PCT values and compared with the Baltimore sepsis score (BSS). There was a significant correlation between the BSS and rise in PCT level. A PCT value of 10ng/ml and increasing suggestive of severe systemic infection even when the blood culture was negative. A cut off value of 3ng/ml and above suggestive of bacterial infection and less than this patients will have better prognosis.[29]

In contrary to all these there are some studies which has shown the negative implications on PCT level compared to other markers. Like the study done by L. Bargues et al , Evaluation of serum procalcitonin concentration in the ICU following severe burn concluded that PCT does not offer a significant advantages for diagnosis of sepsis in burns, compared with the other biological markers such as C-reactive protein (CRP) and white blood count (WBC). In their study CRP has more sensitive and specific in diagnosing the burns sepsis.[30]

# Statistical Analysis

The following statistical analysis were used:

1) Fisher exact test for categorical data.
2) ROC curve to assess the diagnostic performance.
3) t test
4) Mann whitney U test to know the significance.

To analyse the data SPSS software was used.

# Results and analysis

## RESULTS AND ANALYSIS:

Data of 36 patients were analysed with mean age of 27.97 yr (2-59 yr). Among them 44% were male, 42% female and 14% children sustained burns of > 20% TBSA. The average total body surface area of burns was 47.16 (20 – 97 %). Majority of the patients, 86% (31) sustained thermal burns and remaining 14% (05) had electrical burns. Out of 18 patients five patients (27.77%) had lung infection, 08 (44.44%) patients had positive growth of organism in blood culture and 05 (27.77%)patients had local wound sepsis with growth of multiple organisms. The organisms grown in blood culture was Pseudomonas in 3 patients, Klebsiella in 2, Acinetobacter in 01, MRSA in 2.

The diagnostic validity was maximum at the cut off value of 5ng/ml which gives sensitivity – 88.9% and specificity of 83.3% with positive predictive value of 84.2%. To test the significance of PCT in sepsis and non sepsis patients Mann whitney U test was applied and the p – value of < 0.0001 suggest the significant association of PCT in assessing the sepsis. All patients who died had increase in PCT value without any drop. So serial measurement of the PCT has more prognostic value. The cut off value of PCT <5 ng/ml indicates localized infection. If the level started increasing >5ng/ml without any drop one should strongly suspect sepsis in presence of other clinical parameters. All the patients who had MODS (Multi Organ Dysfunction Syndrome) due to uncontrolled sepsis or failure in treatment had PCT levels of >10 ng/ml and increasing further.

## DEMOGRAPHIC PROFILE

Age distribution : Fifteen patients (41.66% ) were in the age group of 21-30yrs with mean age of 27.97

**TABLE : 1**

| Age | n=36 | Percentage |
|---|---|---|
| 0 - 10 yrs | 04 | 11.11 |
| 11-20 yrs | 05 | 13.88 |
| 21-30 yrs | 15 | 41.66 |
| 31-40 yrs | 06 | 16.66 |
| 41-50 yrs | 04 | 11.11 |
| 51-60 yrs | 02 | 5.55 |

Spearmans rank correlation coefficient did not reveal any relationship between age and PCT values.

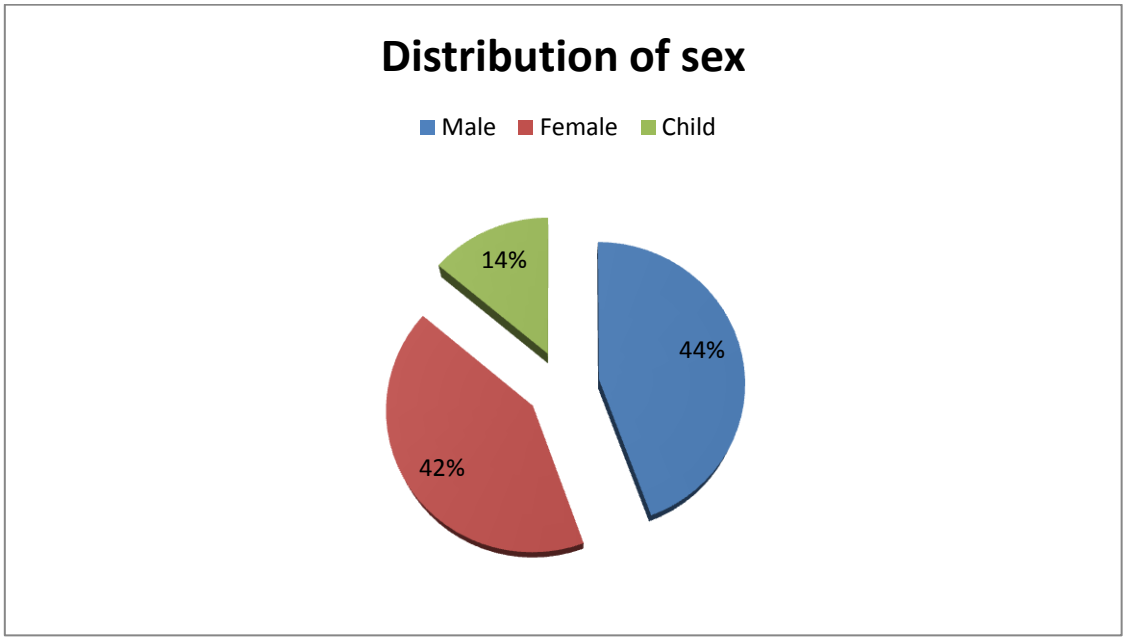
## DISTRIBUTION OF SEX :

Total of 36 cases 16(44%) were male, 15(42%) were female and 05(14%) were children.

**TABLE : 2**

| | Patients | Percentage |
|---|---|---|
| **MALE** | 16 | 44 |
| **FEMALE** | 15 | 42 |
| **CHILDREN** | 05 | 14 |
| **TOTAL** | 36 | 100 |

Fig: 1




Analysis with Mann whitney U test did not reveal any significant relationship between distribution of sex and rise in PCT level.

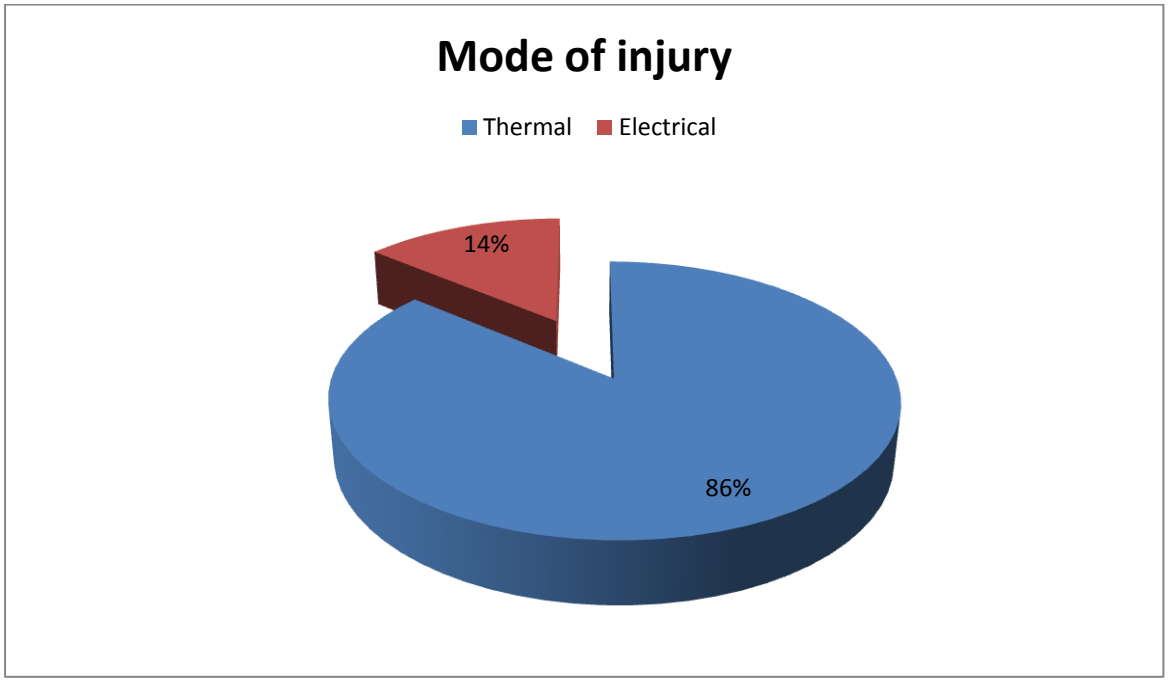
**Mode of injury**

Majority of the patients sustained thermal burns (86%) followed by electrical burns (13.9%).

**TABLE : 3**

| | Number of patients | Percentage |
|---|---|---|
| **Electrical** | 05 | 13.8 |
| **Thermal** | 31 | 86.2 |
| **Total** | 36 | |

Fig: 2



## PERCENTAGE OF BURNS

Twenty seven percent had burns within 30% of Total body surface area. There was no correlation between the percentage of burns and PCT values though higher values were noted in early phase of electrical injuries.

**TABLE : 4**

| % TBSA of burns | n=36 | Percentage |
|---|---|---|
| 21-30 | 10 | 27.77 |
| 31-40 | 04 | 11.11 |
| 41-50 | 08 | 22.22 |
| 51-60 | 07 | 19.44 |
| 61-70 | 03 | 8.33 |
| 71-80 | 01 | 2.77 |
| 81-90 | 02 | 5.55 |
| 91-100 | 01 | 2.77 |

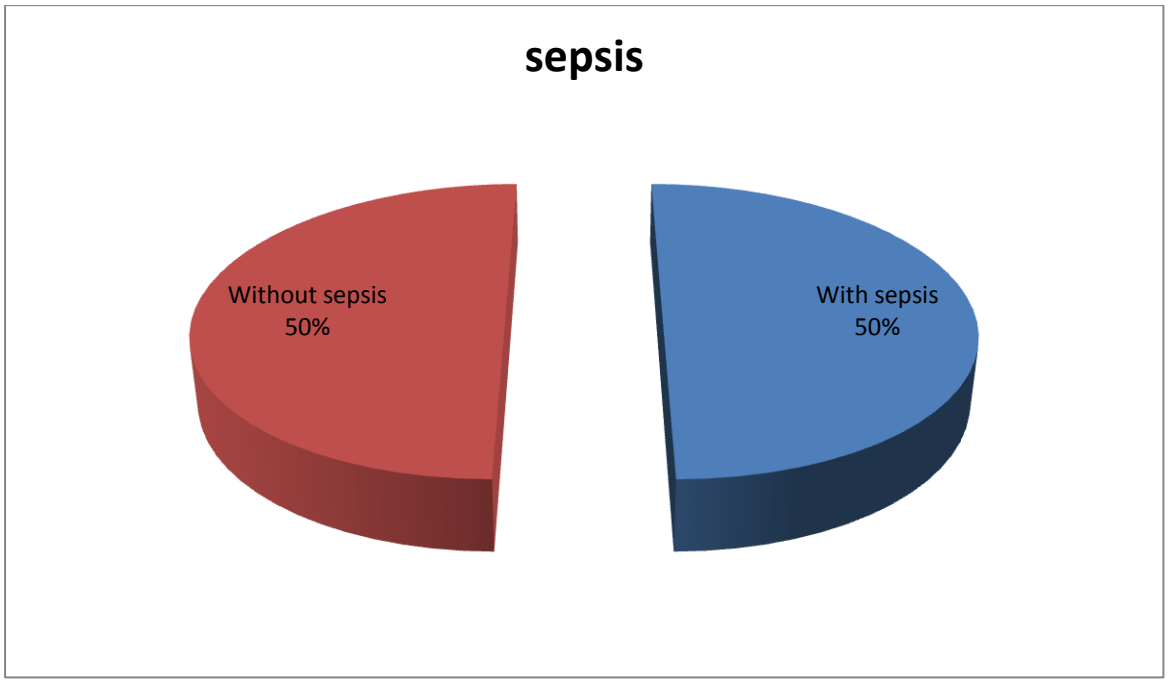
**Development of sepsis in study group:**

**TABLE : 5**

| | Number of patients | Percentage |
|---|---|---|
| **With sepsis** | 18 | 50 |
| **Without sepsis** | 18 | 50 |
| **Total** | 36 | |

Half of the cases 18 (50%) fulfil the criteria for sepsis.

Fig: 3



## Finding cut off value of Procalcitonin using ROC Curve

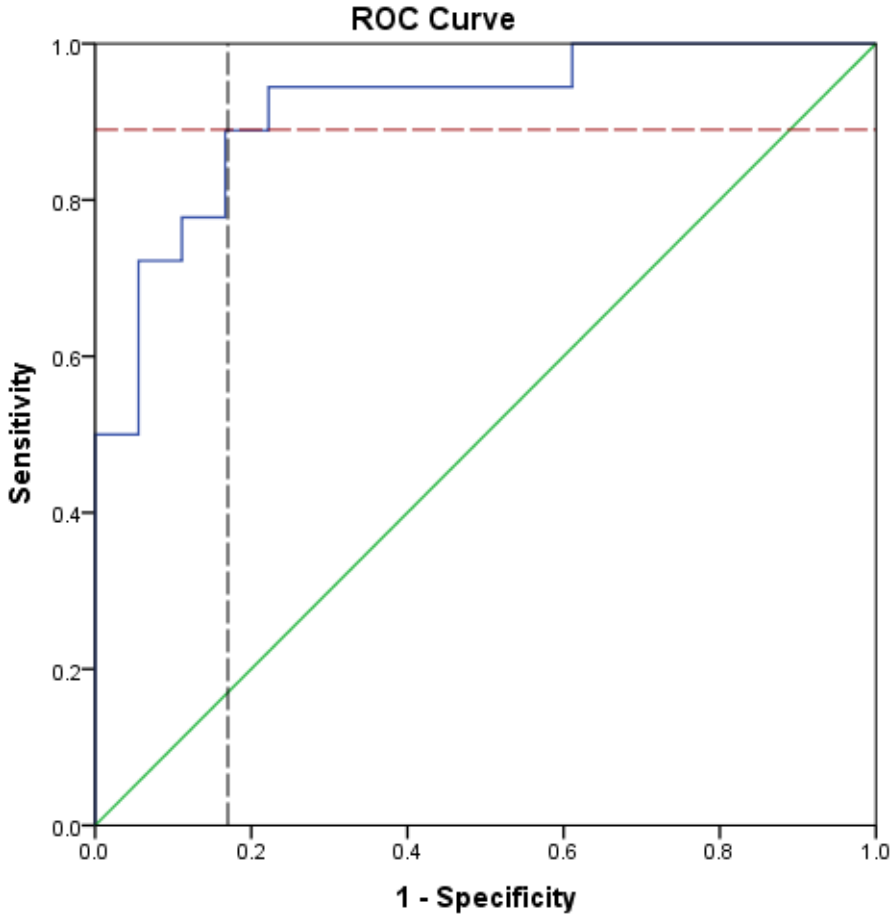



Fig 4, Receiver operating characteristic curve (ROC) showing the diagnostic performance of PCT in sepsis. (Y axis – Sensitivity, X axis – 1- Specificity).

For each PCT value plotted on ROC curve sensitivity and specificity is calculated. The value which is plotted most nearer to the 1 is the cut off value (5ng/ml). Two perpendicular lines were drawn to join X and Y axis which shows sensitivity and 1-specificity to that value.

Sensitivity – 88.9% , Specificity – 83.3%.

**Co-ordinates of the curve :**

**TABLE : 6**

| PCT cut off value | Sensitivity | 1 - specificity |
|---|---|---|
| **3.812** | 0.889 | 0.222 |
| **4.903 (=5)** | 0.889 | 0.167 |
| **5.729** | 0.833 | 0.167 |

The predictive ability of the PCT was determined by using the ROC(Receiver operating curve) and the area under the curve was calculated with 95% confidence intervals. Analysis of the coordinate points reveled the best threshold values of PCT for the prediction of sepsis based on the combination of sensitivity and specificity of each proposed threshold. The cut off value was 5ng/ml based on the ROC analysis with area under the curve of 91%.

**Procalcitonin and sepsis – Testing the significance of association**

**TABLE : 7**

| | | With sepsis (n = 18) | Without sepsis (n=18) |
|---|---|---|---|
| **Mean** | | 43.30 | 3.5 |
| **Median** | | 39.92 | 1.99 |
| **Std deviation** | | 26.65 | 4.03 |
| **Min PCT value** | | 3.25 | 0.1025 |
| **Max PCT value** | | 125 | 15.30 |
| | **25** | 31.06 | 0.89 |
| **Percentile** | **50** | 39.92 | 1.99 |
| | **75** | 49.69 | 5.10 |

**Mann Whitney U test**

**TABLE 8**

**Hypothesis Test Summary**

| | Null Hypothesis | Test | Sig. | Decision |
|---|---|---|---|---|
| 1 | The distribution of procal is the same across categories of sepsis. | Independent-Samples Mann-Whitney U Test | .000[1] | Reject the null hypothesis. |

Asymptotic significances are displayed. The significance level is .05.

[1] Exact significance is displayed for this test.

Analysis with Mann Whitney U test for the relationship between Procalcitonin and sepsis revealed significant correlation (p value < 0.0001) .

**Diagnostic performance of PCT in sepsis :**

**TABLE : 9**

| Variables | | sepsis |
|---|---|---|
| **Cut off value (ng/ml)** | | 5 |
| **Sensitivity (%)** | | 88.9 |
| **Specificity (%)** | | 83.3 |
| **PPV (%)** | | 84.2 |
| **NPV (%)** | | 88.2 |
| **AUC** | | 0.917 |
| **ROC significance** | | 0.0001 |
| **95% CI** | **Lower** | 0.825 |
| | **Upper** | 1.000 |

PPV – Positive predictive value, NPV – Negative predictive value,CI – Confidence interval , ROC – Receiver operating characteristic curve, AUC – Area under ROC,

# Discussion

## Discussion :

How sepsis in burns differ from the sepsis due to other causes ?

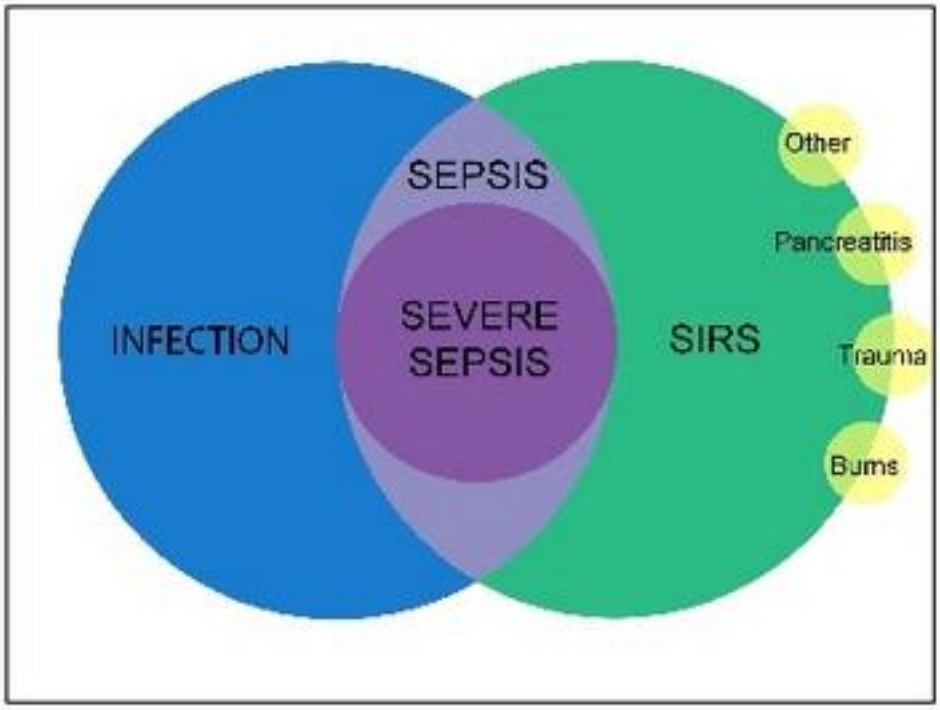



Fig : 6 : Relationship between infection , SIRS and sepsis.

One of the most common cause of sepsis in general population is infection. The cause of infection may be bacterial , viral or fungal. The development of sepsis follows sequence of events. Any infection localized or systemic if not treated leads to development of SIRS. The criteria to define SIRS were mentioned earlier and is due to activation of various inflammatory mediators. SIRS is basically a normal physiologic response of the human body towards a noxious stimulus. If the causative agent is not removed this will cause more exaggerated SIRS and ultimately leads to development of sepsis , severe sepsis and end up with MODS (Multi Organ Dysfunction Syndrome) followed by death as shown in Fig 2.

Though the infection is the primary cause for SIRS this is not always true. There are some conditions where SIRS occur in absence of infection e.g. major trauma, pancreatitis, burns etc. These are the conditions in which body respond to the injury initially by means of SIRS in absence of infection. The severity of the SIRS depends on the initial injury. In cases with major burns the SIRS is invariably followed by infection of the skin. In burns patients SIRS starts initially due to the direct thermal injury to the skin and in later stage it is due to repeated insults caused by infection. So in major burns patients after the resuscitation period it is always difficult to differentiate whether SIRS is a result of injury itself or due to superimposed infection.

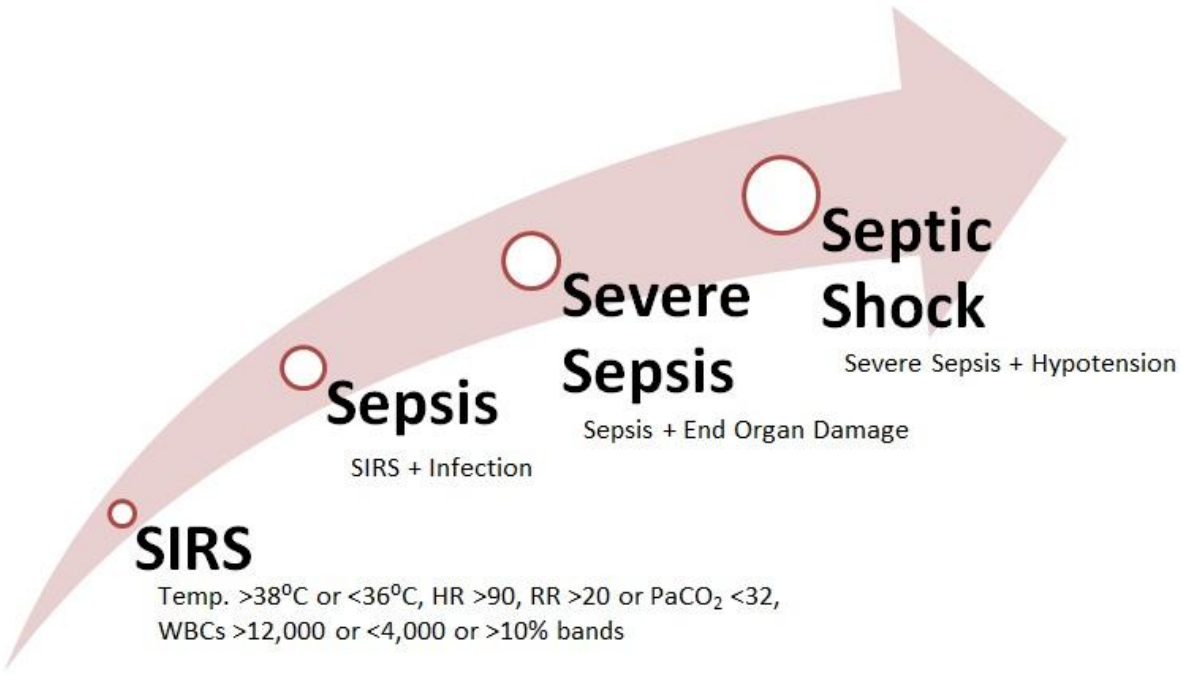



Fig : 7 The events following untreated infection

Routinely diagnoses of sepsis in burns were based on clinical and biochemical factors as explained by the American Burns Association (ABA – 2007). Due to the presence of chronic inflammatory state in burns, the criteria explained by ABA to diagnosis sepsis is either overlooked or under looked. Clinically it is very important to identify systemic infection at the earliest of its stage to initiate antibiotic therapy and to prevent further sepsis . Though blood culture is the gold standard to diagnose systemic infection it will take several days to get the growth of infecting organism and also the presence of negative culture doesn't assure the absence of infection. So it is necessary to identify the indirect circulating markers of systemic infection that can be rapidly assessed and reliable. Many markers were mentioned which is discussed below in briefly.

Markers which are used as sepsis indicators:

1) C- reactive protein
2) Cytokines
3) Adrenomedullin
4) Atrial natriuretic peptide
5) Protein C
6) Endocan
7) Neopterin

C- reactive protein :

In response to infection or inflammation there is an acute phase response in the body which causes change in concentration of many plasma proteins. A plasma protein to designate as acute phase protein its concentration should increase or decrease at least by 25% during inflammatory disorders.[31] C- reactive protein is one of them and the concentration increase by 1000 fold at the time of inflammation. Though the CRP rise at the time of infection or sepsis there are drawbacks to consider it as a potent inflammatory marker. Because CRP doesn't indicate the severity of sepsis, as it increases even in minor infections , doesn't correlate with the severity of host response, its values doesn't differ between survivors and non survivors of sepsis. The increase in concentration at the time of sepsis is not much helpful for the clinical diagnosis as it reaches its peak not before 48hrs after onset of infection and also present in the plasma for a prolonged period even after control of sepsis.[32] CRP is not specific for sepsis as it also rises in some of the non infectious conditions like rheumatic disorders, acute

coronary syndromes, malignancy and after surgery.[33] But one of the promising role of CRP is in assessing the antibiotic response when used to treat localized infections.

**Cytokines :**

Any inflammatory insult cytokines were the primary mediators. These are glycoproteins which are released by macrophages, monocytes, lymphocytes, and endothelial cells. Efforts were made to assess the level of cytokines which can reflect the severity of the inflammation. Tumor necrosis factor-a, IL-1, IL-6, IL-8, and IL-10 are the important cytokines which are considered to assess the sepsis. Among these IL-6 and IL-8 increase by 1000 fold and suppose to be a marker of sepsis.[34] But the major drawback in clinical use is its very short half life of few minutes and the circulating levels falls when it binds with the receptor antagonist.

Adrenomedullin:

The major functions of this molecule is it acts as autocrine, paracrine and endocrine mediators in many biologically significant mechanisms. It helps in protection of organs during sepsis, it has antimicrobial properties against Gram positive and Gram negative organisms. It has role in modulating the complement cascade. This molecule has been considered to play a major role in hyperdynamic state of septic shock. The levels of adrenomedullin correlate well with the sepsis severity score and helps in predicting the septic shock.[35] As the half life of this molecule is about 22 min and it has a binding protein it is very difficult practically to consider in a clinical scenario.

**Atrial natriuretic peptides:**

This secreted by the distension of atria caused by myocardial depression. This plays an important role in regulation of fluid volume. This may become a potential marker but need further evaluation.[36]

**Protein C:**

This is one of the important molecule in coagulation cascade. The concentration of protein c decrease many folds about 12 hrs before the onset of septic shock.[37] It has also been documented that infusion of protein c helps in decreasing 28 day mortality in patients with severe sepsis. In association with prothrombin time, antithrombin activity, and D-dimer which causes worsening of the coagulation cascade on the first day of severe sepsis helps in predicting the organ failure.

**Endocan :**

It is produced when endothelial injury occur which is caused at the time of organ failure and shock in sepsis. It is also called endothelial cell-specific molecule-1 secreted by endothelial cells of lung and kidney at the time of infection in response to cytokines.[38] This helps in regulating cell adhesion in inflammatory disorders and tumour progression. This marker is more sensitive and specific for organ failure so helps in differentiate from patients having only sepsis.

**Neopterin:**

it is released from monocytes after stimulated by interferon. It function is associated with the cytotoxic reactivity of activated macrophages. It is not clinically valuable as marker as the specificity is less between infectious and non infectious causes of sepsis[39] and also long time of induction and accumulation in patients with renal failure.

Thus to define an ideal sepsis marker:

1) It should add to the clinical findings to confirm the diagnosis.
2) It should be able to increase several folds at the earlier stage of the sepsis.
3) The change in its concentration should able to assess the severity of the sepsis
4) It should reflect the response to the treatment
5) It shoud be specific for the infection/sepsis due to bacterial origin.
6) It should differentiate the infectious from non infectious causes.
7) The half life of the marker should be suitable to repeat at regular intervals which are suitable for clinical condition.

So the ideal sepsis marker doesn't exist but which can be more reliable than other markers is the Procalcitonin.

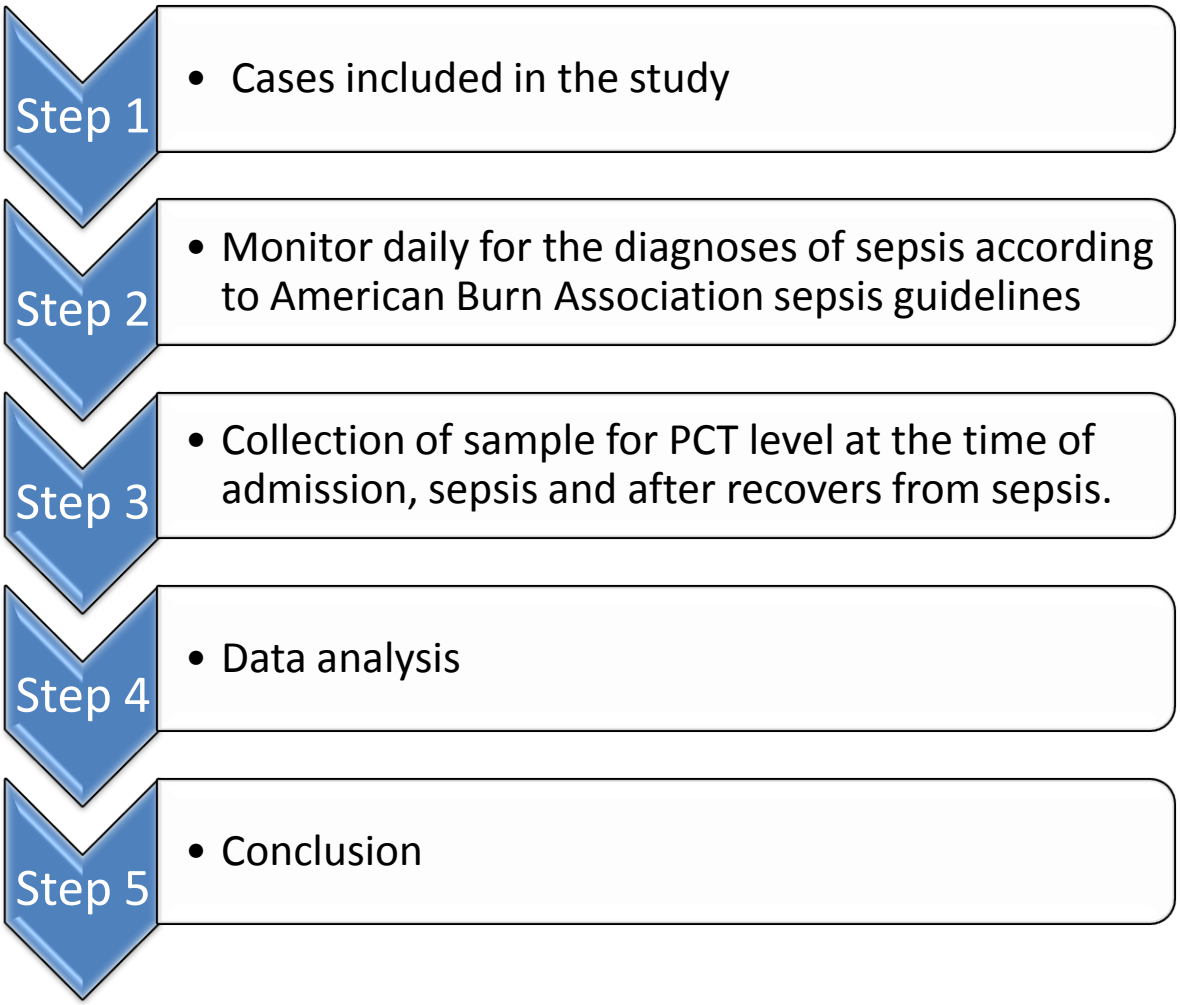
PCT is a 13 kd peptite with a conc of <0.1 ng/ml in healthy individual. Normally secreted by C cell of thyroid gland but at the time of inflammation it is secreted by extrathyroidal tissue liver, lung, kidney, adipocytes and muscle. PCT is used to

differentiate infection from bacterial to non bacterial origin. This was proved by many studies in the past like to differentiate between bacterial from viral meningitis, bacterial pneumonia, fever of unknown origin to rule out etiology of bacterial infection and to rule out sterile v/s infected necrosis secondary to acute pancreatitis. There were various cut off values for each study and sensitivity and specificity were calculated. PCT will also rise in non infective cases as cardiogenic shock, burns, early post operative period, polytrauma, heat shock, severe systemic inflammation e.g., secondary to multiple organ dysfunction syndrome (MODS).

Also the levels of PCT is based on severity of the inflammation with less in SIRS and increased levels at the terminal stages of septic shock.[40] The values of PCT correlate with the SOFA (Sepsis-related organ failure assessment) score[41] and APACHE II (Acute physiology and chronic health evaluation II) score[42] which are the scores of severity of organ dysfunction. The kinetics of PCT is suitable for the clinical assessment. With an half life of 25-30 hr , PCT will start rising 4hr after the infection or injury, peaks at 6hr, attain a plateau for 8-24hrs and will come to base line after 2- 3 days. Serial PCT measurement and the course of PCT over time indicate the disease activity and the prognosis of systemic inflammation respectively. Continuously increasing PCT has more value than the single reading suggestive of disease severity or failure of therapeutic measures.

## ALGORITHM OF THE STUDY PLAN

Fig : 8



# Summary

## Summary :

This was a prospective study done for a period of 9 months to assess the diagnostic validity of procalcitonin (PCT) in sepsis patients due to burns. The criteria given by the American burn association (ABA) for sepsis in burns were used as reference standard. Most of the time in the presence of chronic inflammatory stage the diagnoses of sepsis based on ABA criteria was underestimated and delayed in starting the antibiotic which may lead to mortality of the patient or overlooked the sepsis condition and started antibiotics when it was actually not necessary. This may result in development of resistant organisms. To over come this we need a marker which can reflect the infection status and also add to the diagnostic criteria of sepsis. Various markers had been explained in the past but the PCT was more specific to the infection due to bacterial cause.

A total of 36 patients were included in the study who had burns of > 20%. The vital parameters and necessary investigations which fulfill the criteria of sepsis was done regularly. To know the diagnostic validity we estimated the baseline PCT level at the time of admission or when the patient doesn't have sepsis. When the patient was diagnosed as sepsis one more estimation was done. Data of PCT was collected at the time of sepsis and without sepsis were analysed.

The diagnostic validity of the test, Sensitivity = 88.9%, Specificity= 83.3%, Positive predictive value = 84.2% was calculated. The Sensitivity and specificity was maximum in our study at the cut off value of PCT at 5ng/ml. So patient will have more chances of sepsis with PCT more than 5ng/ml and less when it is <5ng/ml. More than a single estimation serial measurement of PCT has more prognostic value.

The etiology of sepsis in burns patients were local wound sepsis, blood stream infection, urinary infection and respiratory infection. The PCT value in our study was below 5ng/ml when the infection was localized. If the patient was immunologically stable and responded to the antibiotics the PCT level was below 5ng/ml. The onset of sepsis should be suspected when the PCT level started increasing and the level more than 10ng/ml was always had a higher mortality rate which suggests the worsening of sepsis which may led to MODS. The initial PCT level in patients sustained high voltage electrical burns was higher due to trauma and not because of infection.

So the cut off value of PCT mentioned to diagnose sepsis due to other causes is less when compared to burns sepsis patients. This may due to persistent SIRS and localized infection of burn wound which may increase the basal PCT levels. So in case of burns the cut off value to diagnose sepsis is higher than the sepsis due to other causes.

# Conclusion

## Conclusion :

1) PCT has high diagnostic validity to diagnose sepsis in burns patients

   Sensitivity – 88.9%, Specificity – 83.3%.

2) In burns patients the cut off value of PCT to diagnose sepsis is 5 ng/ml.

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# Annexure 1 : Proforma & Consent form

# Annexure 1 : proforma and consent form:

## CONSENT FORM

**Patient information sheet**

All patients presenting with more than or equal to 20% of burns admitting in the burns ward included in the study. The physical and vital parameter changes that occur during sepsis in burns patient will be very marginal as most of the patients are in hypermetabolic response to the injury. The Procalcitonin (PCT) levels rise from the initial level is one of the early parameter in assessing the sepsis in burns patient. We are doing base line PCT level at the time of admission when the patient is free of sepsis. Patient will be monitored continuously for any signs and symptoms of sepsis after admission. Once the patient fulfils the criteria for sepsis then we are repeating the PCT level. Hence PCT level assessed twice, at the time of sepsis and without sepsis. Thus each case will serve his/her own control. Collected data will be dividing in to two groups, i.e : values noted at the time of sepsis and without sepsis. Those of the patients without an episode of sepsis will have a single PCT assay at admission which will serve as a baseline/normal PCT estimation reading. In some cases, patient may have a sepsis episode more than once and we would do PCT check on each episode of sepsis. At the end of the study data will be analysed statistically to find the diagnostic validity of Procalcitonin in burns sepsis patients.

**Please read the details carefully and clarify your queries if any before deciding on consenting for the study.**

What is this study about?

- Study about assessing the diagnostic validity in detecting the sepsis in burns patient.

Does participating in the study alter the treatment of the patient?

- No. The patient shall be given the same treatment as planned irrespective of your decision to agree or disagree to participate in the study.

Does doing this investigation have any side effects?

- No

What investigation will be done if I consent for the study?

- After taking consent a routine blood sample will be taken from the patient to assess the level of Procalcitonin at the time admission, sepsis and post sepsis period.

Will I get compensation if I suffer damage due to the study?

- You are not likely to have any damage because of the study.

What do I have to do?

- You are asked to read this consent form in detail, clarify your doubts if any and sign at the end of the form if you decide to participate in the study.

What will I have to do if I participate in the study?

- You will have to allow to collect a blood sample of about 3 ml for each test during the time of admission for an average of about 2-3 samples and have to respond to the follow-up calls as and when required.

Can I say NO to the study?

- Your participation in the study is completely voluntary and you can choose to either enter the study or not to. Your decision will not alter your treatment in the hospital.

Will my treatment details be kept confidential?

- Your personal and medical records will be kept confidential and shall be used only for academic and research purposes and may be presented or published in academic circles. However, you will not be identified personally.

Can I withdraw from the study once I consent?

- Yes. You can opt out of the study if you want. However, your medical records shall be available for the academic review even if you discontinue the participation.

Can my participation in the study be cancelled by the investigators?

- Yes. Your participation in the study can be rejected or cancelled without your permission or information at any stage during the study period if the investigators wish so for any reason.

**If you have any more queries, please contact Dr.Naveen Kumar H R PHONE: 04162282017 CELL PHONE: 91 9626156754.**

**Informed Consent form to participate in clinical trial**

**Study Title: Prospective analysis of Procalcitonin (PCT) in burns sepsis patients**

**Subject's Name:**

**Age:**

(Subject)

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am

Free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s) [ ]

(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative:_____

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: _____

Signature of the Witness: _____

Date:_____/_____/_____

Name of the Witness: _____

**STUDY : Prospective analysis of Procalcitonin (PCT) in burns sepsis patients .**

**NAME :**

**AGE :**

**HOSPITAL NO :**

**ADDRESS :**

**DIAGNOSIS :**

**TBSA OF BURNS :**

**DOA :**

**DOD/DOE :**

## DATA COLLECTING SHEET :

| DAY | PROCALCITONIN |
|---|---|
| | |
| | |
| | |
| | |
| | |
| | |
| | |
| | |
| | |
| | |
| | |

CULTURE REPORT SHEET :

| DAY | BLOOD CULTURE/URINE CULTURE/SPUTUM CULTURE/PATHOLOGICAL TISSUE | |
|---|---|---|
| | ORGANISM | SENSITIVITY |
| | | |
| | | |
| | | |

# Annexure 2 : Master Chart

# MASTER CHART

| Hosp no | Age | Sex | Date of burns | Date of admission | Percentage of burns | Diagnosis | Pct 1st sample | Pct 2nd sample | Pct 3rd sample |
|---|---|---|---|---|---|---|---|---|---|
| 028192f | 25 | F | 9/11/2012 | 11-sep-12 | 27 | Thermal | 0.2982 | | |
| 013401f | 35 | M | 9/3/2012 | 4-sep-12 | 22 | Electrical | 0.1025 | | |
| 064524f | 59 | F | 10/5/2012 | 7-oct-12 | 61 | Thermal | 0.3951 | 7.969 | |
| 064523f | 55 | F | 11/5/2012 | 7-nov-12 | 58 | Thermal | 0.5045 | | |
| 615516d | 49 | M | 12-may-12 | 12-may-12 | 50 | Thermal | 3.564 | 8.274 | |
| 739071d | 31 | F | 7/17/2012 | 7/17/2012 | 54 | Thermal | 0.244 | 4.374 | |
| 162377c | 47 | M | 8/31/2012 | 8/31/2012 | 44 | Thermal | 1.698 | 5.432 | |
| 089472f | 48 | M | 10/28/2012 | 4-nov-12 | 30 | Thermal | 2.1541 | | |
| 098769f | 30 | F | 11/23/2012 | 24-nov-12 | 33 | Thermal | 1.6441 | | |
| 244196d | 23 | M | 3/1/2012 | 2-mar-12 | 21 | Electrical | 1.0261 | | |
| 133413f | 24 | F | 3/21/2012 | 22-mar-12 | 50 | Thermal | 3.0531 | 10.5 | |
| 956996a | 20 | F | 3/16/2012 | 16-mar-12 | 66 | Thermal | 6.8111 | 41.34 | |
| 174371f | 22 | F | 5-apr-12 | 5-apr-12 | 70 | Thermal | 3.2511 | | |
| 188435f | 9 | M | 4/28/2012 | 29-apr-12 | 60 | Thermal | 7.289 | | |
| 207329f | 29 | F | 5/19/2012 | 20-may-12 | 90 | Thermal | 10.110 | 125.000 | |
| 218428f | 29 | M | 6/4/2012 | 5-jun-12 | 20 | Thermal | 3.147 | 0.523 | |
| 936807 | 35 | M | 6/11/2012 | 11-jun-12 | 27 | Thermal | 15.770 | 6.026 | 1.937 |
| 888851d | 49 | M | 3/11/2012 | 11-mar-12 | 55 | Electrical | 65.600 | 46.620 | |
| 558485c | 13 | F | 7/21/2012 | 22-jul-12 | 25 | Thermal | 1.172 | 1.120 | |
| 777334d | 2 | M | 8/6/2012 | 7-aug-12 | 25 | Thermal | 2.400 | | |
| 265407f | 34 | M | 7/29/2012 | 8-aug-12 | 82 | Thermal | 33.440 | 7.587 | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 261273f | 9 | M | 7/8/2012 | 1-aug-12 | 50 | Thermal | 1.840 | 0.307 | |
| 239446f | 21 | M | 7/4/2012 | 5-jul-12 | 50 | Electrical | 43.130 | 0.694 | |
| 064053f | 40 | M | 10/27/2012 | 10/27/2012 | 58 | Thermal | 2.398 | 10.276 | |
| 631005d | 32 | M | 8/24/2012 | 8/24/2012 | 78 | Thermal | 1.964 | 26.512 | |
| 299400f | 30 | F | 9/17/2012 | 9/17/2012 | 50 | Thermal | 7.791 | 15.300 | |
| 309392f | 22 | F | 9/23/2012 | 28-sep-12 | 40 | Thermal | 5.893 | 1.351 | 31.930 |
| 299612f | 19 | M | 8/30/2012 | 14-sep-12 | 25 | Electrical | 0.270 | | |
| 347792f | 25 | M | 11/22/2012 | 22-nov-12 | 25 | Thermal | 18.330 | 42.430 | 17.970 |
| 338769f | 17 | F | 11/5/2012 | 11/5/2012 | 35 | Thermal | 7.674 | 9.432 | 1.318 |
| 341968f | 5 | M | 11/11/2012 | 20-nov-12 | 40 | Thermal | 2.939 | | |
| 338364f | 26 | M | 11/4/2012 | 11/4/2012 | 45 | Thermal | 1.155 | 0.216 | |
| 857543d | 22 | F | 3/16/2012 | 16-mar-12 | 60 | Thermal | 3.267 | 69.014 | |
| 898831d | 25 | F | 3/12/2012 | 12-mar-12 | 46 | Thermal | 2.643 | 34.349 | 67.854 |
| 895555d | 28 | M | 3/7/2012 | 8-mar-12 | 56 | Thermal | 3.568 | 15.495 | 41.312 |
| 963010d | 18 | F | 6/13/2012 | 6/13/2012 | 97 | Thermal | 4.156 | 10.289 | |

Month Sep. Year 2012

# GRAPHIC (T.P.R.) CHART

Name | Age | Sex | Marital Status | Hospital Number

SUGANTHI S. 299400F 30
C PLS1 Q1W Ward 729H26I CULTIWATER

Service | Ward | Bed | MRD No. | Operation Status

| DATE | 17/9/12 | 18/9 | 19/9/12 | 20/9/12 | 21/9/12 | 22/9 |
|---|---|---|---|---|---|---|
| NO.: OF DAYS | 1 | 2 | 3 | 4 | 5 | 6 |
| DAYS POST - OP. | | | | | | |
| TIME | 4 8 12 4 8 12 4 8 12 4 8 12 4 8 12 4 8 12 4 8 12 2 4 8 10 12 2 4 6 8 10 12 2 4 6 8 10 12 | | | | | |

| PULSE | TEMP C° | TEMP F° |
|---|---|---|
| 210 | 41.1 | 106 |
| 200 | 40.6 | 105 |
| 190 | 40.0 | 104 |
| 180 | 39.4 | 103 |
| 170 | 38.9 | 102 |
| 160 | 38.3 | 101 |
| 150 | 37.8 | 100 |
| 140 | 37.2 | 99 |
| 130 | 36.7 | 98 |
| 120 | 36.1 | 97 |
| 110 | 35.6 | 96 |
| 100 | 35.0 | 95 |
| 90 | RE SP | 60 |
| 80 | | 50 |
| 70 | | 40 |
| 60 | | 30 |
| 50 | | 20 |

| | 17/9/12 | 18/9/12 | 19/9/12 | 20/9/12 | 21/9/12 |
|---|---|---|---|---|---|
| PCT | | | | | 7.791 |
| TC/DC | 19,000 TC | 4700 | 1900 | | 1300 |
| PLT | 4.13 LAC | 3.69 LAC | | | 2.01 LAC |
| RBS | 173 | | 210 | 198 | 201 |
| KCAL | 3800 | 3700 | 3850 | 3900 | 3600 |
| R.Ab | | | | | |
| C/S | | | PUS - NFGNB | | |
| DAY | | | | | |

(Non fermenting gram negative Bacilli)

PCT - PROCALCITONIN
TC/DC - TOTAL & DIF COUNT
PLT - PLATELET
RBS - RANDOM BLOOD SUGAR
KCAL - DAILY INTAKE
R.Ab - RESPONSE TO Ab
C/S - culture / Sensitivity.

Month September Year 2012.

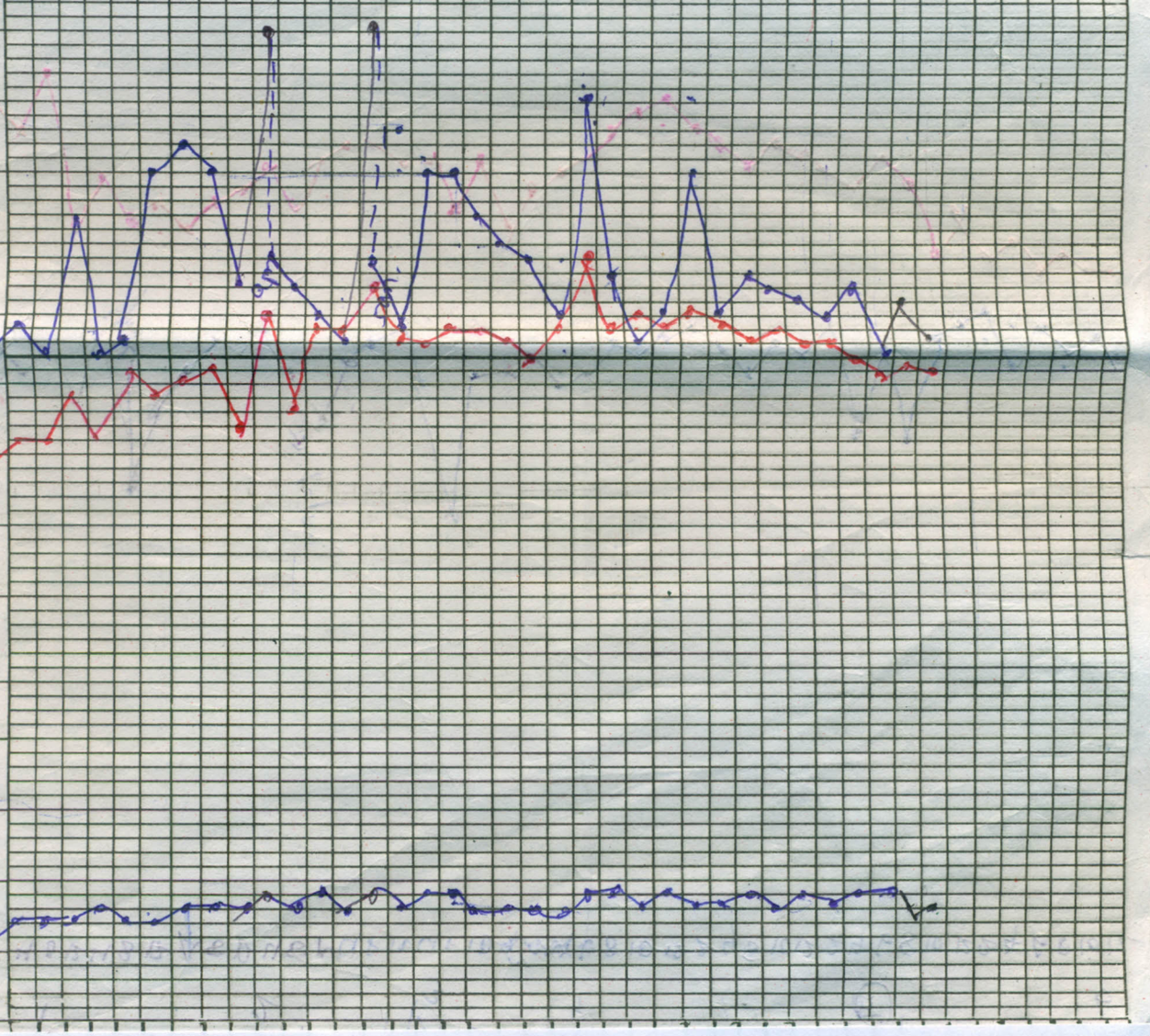
# GRAPHIC (T.P.R.) CHART

SUGANTHI S.
C PLS1 Q1W Ward
299400F 30
7298261 CULTIVATOR F

| Name | Age | Sex | Marital Status | Hospital Number |
|---|---|---|---|---|
| Service | Ward | Bed | MRD No. | ion Status |

| DATE | 22/9/12 | 23/9/12 | 24/9/12 | 25/9 |
|---|---|---|---|---|
| NO.: OF DAYS | 6 | 7 | 8 | 9 |
| DAYS POST - OP. | | | | |
| TIME | 2 4 6 8 10 12 2 4 6 8 10 12 2 4 6 8 10 12 2 4 6 8 10 12 2 4 6 8 10 12 2 4 6 8 10 12 | | | |

| PULSE | TEMP C° | TEMP F° |
|---|---|---|
| 210 | 41.1 | 106 |
| 200 | 40.6 | 105 |
| 190 | 40.0 | 104 |
| 180 | 39.4 | 103 |
| 170 | 38.9 | 102 |
| 160 | 38.3 | 101 |
| 150 | 37.8 | 100 |
| 140 | 37.2 | 99 |
| 130 | 36.7 | 98 |
| 120 | 36.1 | 97 |
| 110 | 35.6 | 96 |
| 100 | 35.0 | 95 |
| 90 | RE SP 60 | |
| 80 | 50 | |
| 70 | 40 | |
| 60 | 30 | |
| 50 | 20 | |
| 40 | 10 | |



| | 22/9/12 | 23/9/12 | 24/9/12 |
|---|---|---|---|
| PCT | | | 15.30 |
| TC/DC | 2200 | 3200 | 1300 |
| PLT | " | 1.96 lac | |
| RBS | 160 | | 268 |
| KCAL | 3300 KCal | 3500 | 3100 2800 |
| R.Ab | | | NIL |
| C/S | | | Klebsiella in Blood. |
| DAY | | | |

PCT - PROCALCITONIN
TC/DC - TOTAL & DIF COUNT
PLT - PLATELET
RBS - RANDOM BLOOD SUGAR
KCAL - DAILY INTAKE
R.Ab - RESPONSE TO Ab
C/S - culture / sensitivity.

Month ____ Year 2012 **GRAPHIC (T.P.R.) CHART**

| Service | Age | Sex | | | Hospital Number |
|---|---|---|---|---|---|
| | SATHYA . S | | 898831D 25 | F | |
| | C PLSB Q1W Ward | | 5789391 LABOURER | H | Occupation Status |

DATE: 24/3/12 | 25/3/12 | 26/3/12 | 27/3/12

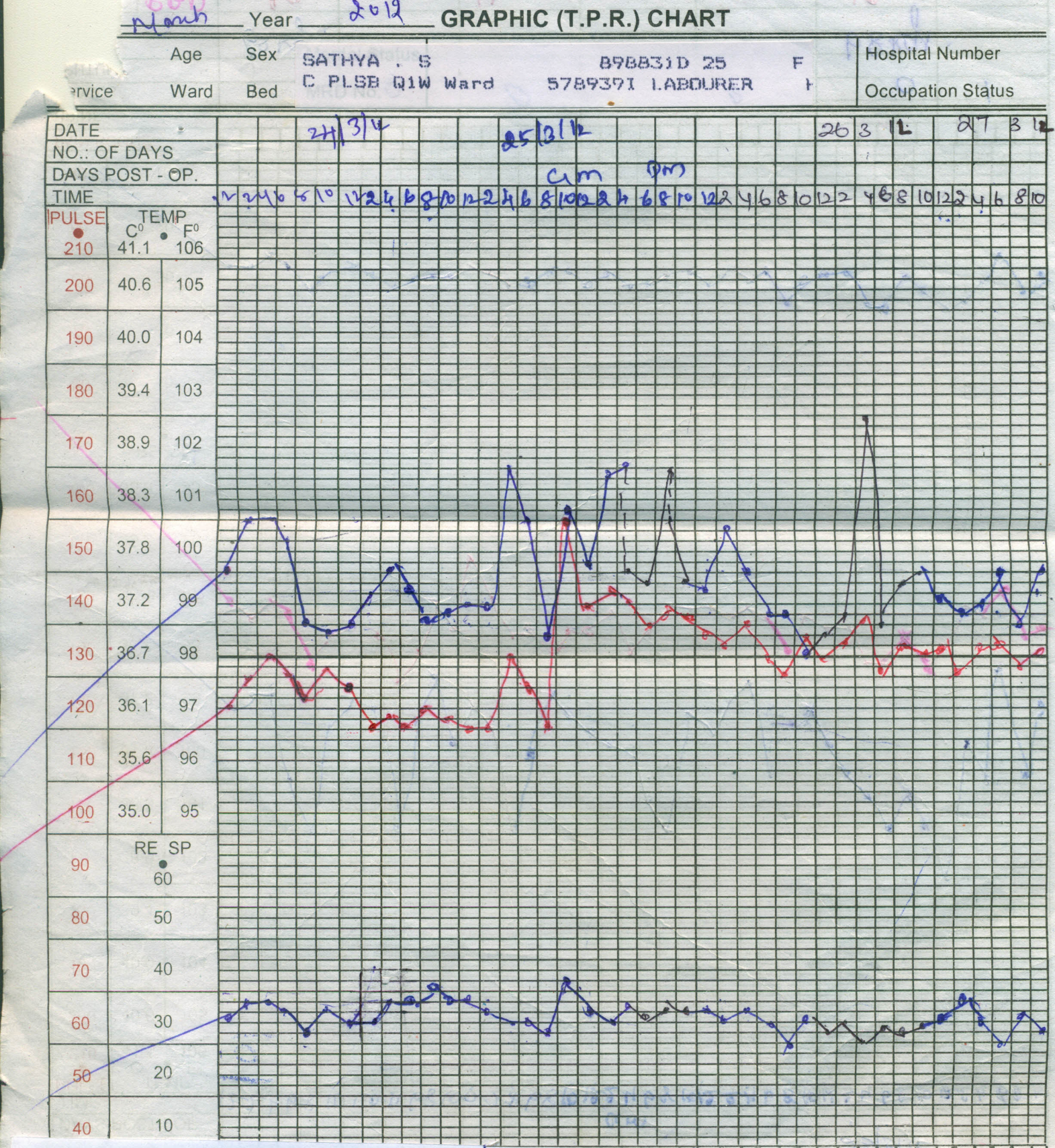
NO.: OF DAYS

DAYS POST - OP.

TIME: 12 2 4 6 8 10 12 2 4 6 8 10 12 2 4 6 8 10 12 2 4 6 8 10 12 2 4 6 8 10 12 2 4 6 8 10

AM PM

| PULSE | TEMP C° | TEMP F° |
|---|---|---|
| 210 | 41.1 | 106 |
| 200 | 40.6 | 105 |
| 190 | 40.0 | 104 |
| 180 | 39.4 | 103 |
| 170 | 38.9 | 102 |
| 160 | 38.3 | 101 |
| 150 | 37.8 | 100 |
| 140 | 37.2 | 99 |
| 130 | 36.7 | 98 |
| 120 | 36.1 | 97 |
| 110 | 35.6 | 96 |
| 100 | 35.0 | 95 |
| 90 | RE SP | 60 |
| 80 | | 50 |
| 70 | | 40 |
| 60 | | 30 |
| 50 | | 20 |
| 40 | | 10 |



| | 24/3/12 | 25/3/12 | 26/3/12 | 27/3/12 |
|---|---|---|---|---|
| PCT | | 34.349 | | |
| TC/DC | 8000 | | 6000 | |
| (lac) PLT | 2.12 lac | 1.98 lac | 1.87 | |
| RBS | 162 | | 148 | |
| KCAL | 2800 | 2600 | 2200 | 2700 |
| R.Ab | | | Nil | |
| C/S | | Multiple organisms in pus c/s | | |
| DAY | | | | |

PCT - PROCALCITONIN
TC/DC - TOTAL & DIF COUNT
PLT - PLATELET
RBS - RANDOM BLOOD SUGAR
KCAL - DAILY INTAKE
R.Ab - RESPONSE TO Ab
C/S - culture / sensitivity

Month 28 Year 2012 **GRAPHIC (T.P.R.) CHART**

| Name | Age | Sex | Marital Status | Hospital Number |
|---|---|---|---|---|
| SATHYA . S | | | B98831D 25 F | |
| Service | Ward | Bed | C PLSB Q1W Ward | 5789391 LABOURER Occupation Status |

DATE: 27/3/12 — 28/3/12 — 29/3/12 — 30/3/12

NO.: OF DAYS

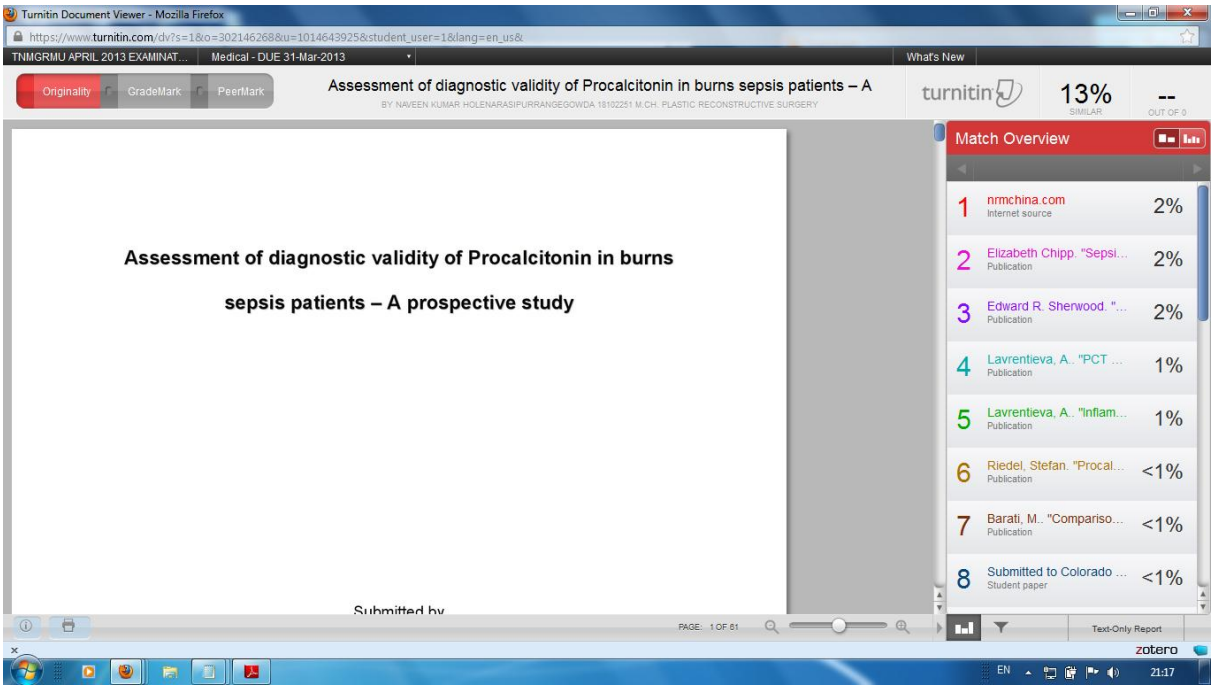
DAYS POST - OP.

TIME: 12 2 4 6 8 10 12 2 4 6 8 10 12 2 4 6 8 10 12 2 4 6 8 10 12 2 4 6 8 10 12 2 4 6 8 10

| PULSE | TEMP C° | TEMP F° |
|---|---|---|
| 210 | 41.1 | 106 |
| 200 | 40.6 | 105 |
| 190 | 40.0 | 104 |
| 180 | 39.4 | 103 |
| 170 | 38.9 | 102 |
| 160 | 38.3 | 101 |
| 150 | 37.8 | 100 |
| 140 | 37.2 | 99 |
| 130 | 36.7 | 98 |
| 120 | 36.1 | 97 |
| 110 | 35.6 | 96 |
| 100 | 35.0 | 95 |
| 90 | RE SP | 60 |
| 80 | | 50 |
| 70 | | 40 |
| 60 | | 30 |
| 50 | | 20 |
| 40 | | 10 |

| | 28/3/12 | 29/3/12 | 30/3/2012 |
|---|---|---|---|
| PCT | | 67.854 | |
| TC/DC | 4000 | 5000/cumm | 3200 |
| PLT | | 1.02 Lac. | 98000 |
| RBS | | 252 | |
| KCAL | 2100 | 1800 | 1750 |
| R.Ab | | NIL | |
| C/S | | Blood culture Negative | |
| DAY | | | |

PCT - PROCALCITONIN
TC/DC - TOTAL & DIF COUNT
PLT - PLATELET
RBS - RANDOM BLOOD SUGAR
KCAL - DAILY INTAKE
R.Ab - RESPONSE TO Ab
C/S - culture / Sensitivity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