C-REACTIVE PROTEIN AS AN INDEPENDENT PREDICTOR OF SEVERITY   IN COMMUNITY ACQUIRED PNEUMONIA

Submitted By

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in

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Under the guidance of

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2011

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I hereby declare that this dissertation entitled **"C-REACTIVE PROTEIN AS AN INDEPENDENT PREDICTOR OF SEVERITY IN COMMUNITY ACQUIRED PNEUMONIA"** is a bonafide and genuine research work carried out by me under the guidance of **DR.M.S.BIRADAR** M.D. Professor and HOD Of Medicine.

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LIST OF ABBREVATIONS

BEP - Bilateral extensive pneumonia

CAP - Community acquired pneumonia

CRP - C-reactive protein

CEF-S - Ceftriaxone+Sulbactum

LEP - Left sided extensive pneumonia

LEVO - levofloxacin

LLLP - Left lower lobe pneumonia

LULP - Left upper lobe pneumonia

MOF - Multiorgan failure

ORNI - Ornidazole

PIP+TAZ - Pipericillin+Tazobactum

REP - Right sided extensive pneumonia

RMLLP - Right middle and lower lobe pneumonia

RMLP - Right middle lobe pneumonia

RLLP - Right lower lobe pneumonia

RUMLP - Right upper and middle lobe pneumonia

RULP - Right upper lobe pneumonia

ABSTRACT

Background and objective :CRP being a acute inflammatory marker demonstration of its serial rise in patients with CAP predicts the severity and outcome in these patients . We aim to study CRP levels on the day of admission and day 4, which can predict 30 day mortality, need for mechanical ventilation and or inotropic support, and development of complicated pneumonia in CAP patients. This study was done with a objective to find out whether C-reactive protein is an independent predictor of severity in community acquired pneumonia.

Material and methods: 100 consecutive patients presented with Community Acquired Pneumonia admitted to Shri B.M.Patil Medical College Hospital and Research Centre, Bijapur from October 2008 to May 2010 were included in this study. Detailed history was taken. Detailed clinical examination was done. sputum examination and chest x-ray and other relavent investigations done. CRP levels were estimated on admission and day-4 by immunoturbidimetric method.

Results: : In this study we observed that community acquired pneumonia is more common in middle aged males. Most common is combined right middle lobe and lower lobe pneumonia.

Commonest organism isolated among culture positive patients was klebsiella pneumonia(14%) followed by staphylococcus areus(12%) then streptococcus pneumonia(5%). How ever 65% patients sputum was sterile.

CRP levels are increased in 30% and decreased in 70% patients, on day-4 when compared to the levels on day-1.

Worsening of CAP occurred in 10(33.3%) patients among the group in which CRP had raised on day four and 3(4.28%) patients among the group in which CRP had decreased on day 4.

Mean duration of stay, need for mechanical ventilatory support, inotropic support, complications, and mortality was seen higher in the group with raise in day -4 CRP levels.

Conclusion: This study concludes that if CRP levels raises on day-4 when compared to day-1, the length of stay in hospital, need for mechanical ventilator support, complications, and mortality increases**.** C-reactive protein is an independent predictor of severity in community acquired pneumonia.

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INTRODUCTION

Community acquired pneumonia [CAP] continues to be a common respiratory disorder in developing countries like India.

Evidence suggest that in many cases physicians overestimate the severity of community acquired pneumonia, leading to unnecessary admissions, where as others suggests that initial assessment may underestimate the potential severity of CAP. This has lead to the development of a number of severity scores and prediction rules.

It is well recognized that elevated concentrations of acute phase reactants correlate with the severity and outcome of sepsis and it has been shown that elevated CRP is an independent predictor of mortality in acutely ill patients.

Serial CRP level estimation can be taken as a marker of severity of CAP and as a marker of treatment response.

OBJECTIVE OF STUDY

To find out whether C-reactive protein is an independent predictor of severity of community acquired pneumonia.

REVIEW OF LITERATURE

Historical Review:

Pneumonia has been recognized for many centuries. Pneumonia was described by Hippocrates in fourth century B.C.[1]Louis Pasteur, French scientist and bacteriologist is credited with definite discovery of pneumococcus (1881). Joseph parrot, French physician gave the description of pneumococcus (1881). Friedlander, between 1881-1884 first found bacteria in the lungs of fatal cases of pneumonia using the staining of his colleague Gram.

Albert Fraenkel German physician established that pneumococcus is the causal agent in lobar pneumonia (1884). Several years later Fraenkel and W Selbaum identified different serological types of pneumococci. Albert Bruce Sabin (1906) devised a rapid 'stained slide test' for typing of pneumococci (1902), which is known as 'Sabins rapid method'. Thomas Francies Ji. American pathologist (1901) developed a skin test to determine the presence of antibodies in pneumococcal pneumonia known as the 'Francies Test' carl Friedlander, German pathologist is credited with isolating Klebsiella pneumoniae, the causative agent of Friedlanders pneumonia in 1883. Rene T.H. Laennec, liench physician gave the first classical description of the pathological changes and auscultatory signs in pneumonia (1819) Gallon carl Rokitansky was the first to differentiate between lobar and bronchopnueumonia.[1]

L.E.H whitley in 1938 introduced sulphonamides in the treatment of pneumonia and reduced the mortality rate considerably. The discovery of antibiotics revolutionized the concept of chemotherapy and penicillin later.

In 1961 Channock and his associates succeeded in cultivating Eaton agent on cell free media and positively identified it as PPLO or mycoplasma. Since then Eaton PPLO be named as mycoplasma. In 1976 the first epidemic of Legionnaires disease was diagnosed in Philadelphia. Later it was named as Legionella pneumophila. The recognisation of acquired immunodeficiency syndrome (AIDS) in 1979, in New York and California among health homosexual has brought the problems of diagnosis and management of pneumocystis carnii pneumonia to a wider audience In Britain PCP was recognized in 1959 as the cause of interstitial pneumonia carrying high mortality.

The most recent event has been the description in 1986, of pneumonia caused by a new a typical pathogen chlamydia pneumoniae.[1]

Anatomy:

Structure of Alveolar epithelium:

The microscopic structure of alveolar walls consists of;

a. The capillary endothelium.

b. The basement membrane and surrounding interstitial tissue.

c. The alveolar epithelium- consists of two principal cells.

1. Flattened, plate like pavment type-I pneumocytes

2. Granular cells which exhibit surface microvilli and contain Osmophilic lamellated inclusion bodies, type-II pneumocytes.

Type-II cells: important source of pulmonary surfactant which prevents collapse of alveoli.

The alveolar walls are not solid but are perforated by numerous pores of Kohn which permit the passage of bacteria and exudate between adjacent alveoli. Pulmonary surfactant: it is mostly phosphatidylcholine (Lecithin) which coats the alveolar cell membrane and is glycoprotein biochemically[2]

Structure of tracheobronchial tree:

The entire respiratory tree except vocal cords is lined by pseudostratified, tall columnar, ciliated epithelial cells, heavily admixed with mucous secreting goblet cells. There are 8 epithelial cell types in man

1. The Basal Cell:

Divides and daughter cells pass to the superficial layer.

2. The Intermediate Cell: This is columnar, probably processor that differentiates in to the ciliated cell, the brush cell, the clara cell or goblet cell.

3. The Ciliated Cell: The cilia are now known to have double pairs of axonemes and a special axoneme in the center.

4. The Brush Cell: Resembles a similar cell found in the gut and in the nasal sinuses.

5. The Clara Cell: It also contains small, discrete, election dense granules. These are the

more common secreting cells of the airways. The mucous moistens the inspired air, prevents drying of delicate alveolar walls and traps dust and paniculate matter.

6. The Kulchitsky Cell: Contains numerous neuro secretary granules.

7. The Mucus Cell: Is a secretary cell containing numerous huge and confluent secretary granules.

8. The Serous Cell: Resembles the semus cell of the submucosal gland and contains small, discrete, electron dense secretary granules. The Bronchiolar surface is covered with cilia which are surrounded by a protein layer rich in lysosyme and immunoglobulins, but unlike the alveoli the surface layer contains no surfactant and, unlike the bronchi, no mucous. Indeed, there are no mucus cells in the walls of bronchioles, instead non ciliated granulated clara cell secret the mucus.

Definition: Pneumonia[3]

When the word pneumonia is used in medical practice, it almost always refers to syndrome caused by acute infection, usually bacterial, characterized by clinical and radiographic signs of consolidation of a part or parts of one or both lungs. However, the use of the term has been greatly extended to include non bacterial infection of the lungs caused by a wide variety of micro organisms. Pneumonitis is occasionally used as a synonym for pneumonia, particularly when inflammation of the lung has resulted from a non-infections cause, such as chemical or radiation injury.

Classification[4] :

Anatomical Classification

a. Lobar pneumonia,

b Segmental pneumonia

c Subsegmental pneumonia

d Bronchopneumonia

Empirical Classification:

a. Community acquired pneumonia

b. Hospital acquired (nosocomial) pneumonia.

c. Aspiration pneumonia

d Immuno-compromised host pneumonia

Behavioral Classification:

a Easy pneumonia (Responds to initial treatment)

b. Difficult pneumonia (fails to do so)

MICROBIOLOGICAL CLASSIFICATION

1. Pneumococcal pneumonia .Leptospiral pneumonia, Streptococcus pneumoniae , Pasteurella multocida

2. Atypical pneumonia Streptococcus pyogenes, Legionella spp (Legionnaries), Neisseria meningitides , Mycoplasma pneumonia, Brucella spp ,Chlamydia spp, Francisella tularensis , Coxiella burnetti (Q fever) Rickettsial pneumonias

3. Staphylococcal pneumonia, Listerial pneumonia, Staphylococcus aureus Pseudononas pseudomallei ,

4. Gram-negative enteric Bacillus anthracis pneumonia. Actinomycotic and nocardial

   Klebsiella spp pneumnia , Pseudomonas aerugionosa , Escherichia coli , Enterobacter spp

   Serratia spp .

5. Haemophilus influenzae pneumonia

6. Moraxella catairhalis pneumonia

7. Anaerobic pneumonia (mixedflora) , Bacteroides spp , Fusobacterium spp , Peptococcus spp , Peptostreptoccus spp.

8. Mycobacterial pneumonia , Mycobacteriurn tuberculosis.

Non Bacterial pneumonia:

Viral pneumonia

I. Influenza

II. Measles

III. Adenovirus

IV. Varicella

V. Cytomegalovirus

VI. Respiratory syncytial virus

VII. Parainfluenza virus

VIII. Coronavirus

IX. Coxsackie virus

X. Rhino virus

XI. Epstein - Barr virus

XII. Herpes simplex virus

XIII. Hantavirus

Fungi

Actinomycotic pneumonia

Parasitic pneumonia

Chemical pneumonia

Physical pneumonia e.g. ionising radiation.

Bacteriology

The microbial etiology in case of pneumonia is determined in less than 50% of cases despite extensive diagnostic testing.The five most frequent pathogens were Streptococcus pneumoniae 29%, Haemophilus influenzae 11%, influenza virus A and B 10%, Legionella spp 8%, chlamydia pneumonia 7%, Gram negative enteric bacilli(GNEB)accounted for 6% and pseudomonas aeuruginosa for 5%.[5]

Streptococcus pneumonia[6] :

Gram positive,capsulated, ovoid or lanceolate cocci arranged in pairs or short chains. Pneumococci have complex growth requirement, growth occur only in media containing fermentable carbohydrate or enriched with blood or serum. On blood agar after incubation for 24 hours the colonies are small (0.5-1 mm) circular, raised semitransparent, shiny growth and hemolysis are promoted by 5% to 10% CO_2.

H. Influenzae:

H. In fluenzae is a small to medium seized, Gram negative, non motile, non sporing coccobacilli. The bacilli have fastidious growth requirements. The accessory growth factors like X and V present in the blood are essential for growth. The colonies of H.influenzae will be large and well developed alongside the streak of staphylococcus and smaller further away. This phenomenon is called satellitisrn[6] .

Legionella pneunophila:

Short rods, occasionally filaments gram negative, non sporing, motile. Legionellae requires cystine and iron for primary isolation, Charcoal yeast extract agar containing antibiotics to suppress the growth of other organism may be used[6].

Klebsiella pneumonia, Enterobacter aerogenes, Escherichia coli:

The coliform bacteria are gram negative rods, non-sporing, often motile, forms in chains. On agar the colonies are relatively large with an average diameter of 2-3 mm, circular raised and low convex with an entire edge and smooth surface, they may flatter with more irregular surface and a more effuse and irregular edge or they may assume vine leaf form Capsules are rare in E-coli, more frequent in enterobacter and large, irregular in Klebsiella.

All members of Enterobacteriaceae, with the exception of a few klebsiella grow in the presence of bile salts and given rise to colonies on Mac Conkey's agar nearly as large as those on nutrient agars. Many members of the genus klebsiella when isolated form typically mucoid colonies[6].

Staphylococcus aureus:

Staphylococci are gram positive cocci that occur in grape like clusters. The two principal species are staph. aureus and staph epidermidis on nutrient agar they form smooth, circular opaque often yellow pigmented colonies, 1-2 mm in diameter. The growth of staph.aureus is butyrous and easy to emulsify but staph.epidermidis is sometimes gelatinous and difficult to emulsify. A colony of staph aureus (but not staph epidemidis) suspended in broth containing diluted rabbit plasma produce an extracellular enzyme, coagulase, which cause the plasma to clot in four hours. All strains that elaborate coagulase are defined as staph aureus even if they fail to produce pigment[6].

Streptococci:

The streptococci are spherical gram positive arranged in chains or pairs. On blood agar the colonies are small 0.5-1 mm, circular. Semitransparent low convex discs with an area of clear hemolysis around them Based on action on red blood cells, resistance to physical and chemical factors, biochemical tests streptococci are classified as;

1. Beta hemolytic streptococci.

2. Alpha Hemolytic streptococci.

3. Gamma or non-Hemolytic streptococci.

Mycoplasma:

Gram negative, smallest free living organism and highly pleomorphic. They occur as granules and filaments of various sizes. The granules may range from 100-1000 um in size, with coccoid, balloon, disc, ring or solid forms mycoplasma may be cultivated in fluid or solid media, media for cultivating mycoplasma are enriched with 20% horse or human serum and yeast extract, penicillin and thallium acetate are added as selective agents. The colony is typically biphasic, with a fried egg appearance.

Chlamydia pneumonia:

Gram negative, spherical particle 200-300 nm in diameter The cell wall is fragile and pliable, leading to pleomorphism. Chalmydia stains well with Giemsa, castaneda, machiavello or Gimsae stains[6].

Pseudomonas aeruginosa:

Gram negative straight or slightly curved rods motile by means of one or more polar flagella, non sporing and not acid fast. It grows readily on culture media and forms smooth round colonies with a fluorescent greenish colour. Some strains hemolyze blood.

Citrobacter:

Motile aerobic gram-negative rods belong to the slow lactose fermenting coliform bacilli. They grow well on ordinary media producing smooth convex colonies 2-4 mm in diameter on nutrient agar. They are not pigmented, rough or mucoid forms sometimes occur.

Anaerobes:

Anaerobes form the predominant organisms of the oropharynx. The predominant anaerobes found are peptostreptococcus. Bacteroides melamnogenicus, microaerophilic streptococci, bacteroides fragilis.

Bacteroides:

Non spore forming, strictly anaerobic, gram negative bacteria. They grow on complex media eg : Brain-heart infusion agar in an anaerobic atmosphere containing 10% CO_2. Most common are B melaninogenicus, B oralis, B fragilis.

Proteus:

Proteus produces urease and hydrolyses urea with liberation of ammonia. It tends to swarm spreading rapidly over the surface of solid media does not grow well at on acid pH.

PATHOGENESIS

Pneumonia is predisposed by any condition that:

i.   Reduces or suppresses the cough.

ii. Impairs mucociliary activity.

iii. Reduces the effective phagocytic activity of alveolar macrophages and neutrophils.

iv. Impairs immunoglobulin production.

Potential pathogens reach the lung to cause pneumonia chiefly by microaspiration of secretions containing oropharyngeal flora also by inhalation from environment, from nebulizer or anaesthetic circuit and by blood spread. Sometimes pathogens may spread from an adjacent extrapulmonary site of infection such as mediastinum, spine, chest wall or abdominal cavity.

Aspiration and microaspiration:

Aspiration of small amounts of oropharyngeal contents is known to occur in healthy people during sleep. This tendency is increased by states in which the ability to cough is depressed or otherwise impaired such as following surgery, general anaesthesia, tracheostomy or the passage of an endotracheal tube or nasogastric tube.

The intrinsic defences of the lungs may be unable to cope with the inoculum if it contains particularly pathogenic organisms or if there are sufficiently large numbers of less pathogenic organisms. Favourable conditions for infection may also be provided by chemical injury to the lungs resulting from overt gastric acid aspiration or by pulmonary oedema and alcoholism is an important predisposing factor.

Inhalation:

The inhalation of microbes contained in small particle aerosols is thought to be important in the transmission of viral infections and also in legionella pneumonia. The inhalation of infected particles from animals may be responsible for psittacosis and coxiella pneumonia. Patient-to-patient spread may occur by both direct contact (via fomites) and droplet spread. Pathogens may also be introduced to the lower respiratory tract by contaminated nebulizer circuits or other respiratory equipment.

Colonization:

The lower respiratory tracts of patients with pre-existing lung diseases, such as chronic bronchitis, emphysema, bronchiectasis and cystic fibrosis, may become colonized by potentially pathogenic organisms, which may cause acute exacerabations of infections including pneumonic consolidation from time to time.

Blood spread:

Occasionally, pneumonia may result from the haematogenous spread of bacteria from a focus of infection elsewhere. This may occur with Gram negative and staphylococcal bacteraemia. Patients with intravenous cannulae, temporary pacing wires and those receiving chronic haemodialysis are particularly susceptible.

PATHOLOGY

In 1834 Laennec described the stages of consolidation. Lobar Pneumonia is a wide spread fibrinosuppurative consolidation of large areas and even whole lobes of the lung and evolved through four stages: congestion, red hepatization, grey hepatization and resolution.

During the stage of congestion, the affected lobe(s) is (are) heavy, red and boggy. Histologically vascular congestion can be seen with proteinaceous fluid, scattered neutrophils, and many bacteria in the alveoli within a few days the stage of red hepatization ensues, in which the lung lobe has a liver- like consistency. The alveolar spaces are packed with neutrophils, red cells and fibrin. In the next stage grey hepatization the lung is dry, gray and firm, because the red cells are lysed, while the

fibrinous exudate persists within the alveoli. Resolution follows in uncomplicated cases as exudate within the alveoli are enzymatically digested and either resorbed or expectorated[9].

The pleural reaction may similarly resolve or undergo organization, leaving fibrous thickening or permanent adhesions.

Bronchopneumonia:

In this pattern, foci of inflammatory consolidation are distributed in patches throughout one or several lobes most frequently bilateral and basal, well-developed lesions up to 3 or 4 cm in diameter are slightly elevated and are gray red to yellow. Pleural involvement is less common. Histologically, the reaction consists of focal suppurative exudate that fills the bronchi, bronchioles, and adjacent alveolar spaces.

Interstitial pneumonia: Interstitial pneumonia is defined by histopathologic identification of an inflammatory process predominantly involving the interstitium, including the alveolar walls and the connective tissue around the bronchovascular tree. The inflammation may be patchy or diffuse. The alveolar septa contain an infiltration of lymphocytes, macrophages, and plasma cells. The alveoli do not contain a significant exudate, but protein rich hyaline membranes may line the alveolar spaces[9].

Miliary pneumonia: The concept of miliary pneumonia is based on its numerous discrete lesions resulting from the spread of the pathogen to the lungs via blood stream. The varying degrees of immunocompromise in miliary tuberculosis, histoplasmosis,

coccidioidomycosis manifests are variations in the tissue reaction, (from granulomatous with caseous necrosis to foci of necrosis), the fibrinous exudate, and the weak, poorly formed cellular reaction[10].

Risk Group[10]:

1. Patients of Alcoholism[11].

2. Smoking[12].

3. Patients of diabetic ketoacidosis

4. Patients of COPD

5. Bronchiectasis

6. HIV infection-> CD4 count <200/microliter.

7. Dementia, stroke, altered level of conscious.

8. Sickle cell disease.

9. Solid organ transplantation.

CLINICAL FEATURES [3]

The clinical features of pneumonia (symptoms, signs and radiologic findings) can not be reliably used to establish the etiologic diagnosis of pneumonia with adequate sensitivity and specificity. Although, in some circumstances, clinicians can confidently use clinical features to establish a specific etiologic, diagnosis in the majority of cases this is not possible[13].

Pneumococcal pneumonia: Most common bacterial pneumonia. The onset of illness frequently proceeded by mild coryza or other upper respiratory tract symptoms and begin

abruptly with high graded fever, rigors or shaking chill, pleuritic chest pain, productive cough, often rusty brown[3].

Haemophilus inflnenzae: Onset is insidious, it usually but not invariably occurs in patients, often elderly with exacerbations of underlying lung disease such as chronic bronchitis or asthma. It may also occur in association with alcoholism or in patients with impaired immunity, including those with HIV infection[3].

Legionella pneumonia: The median age of infection is 55 years, symptoms begin with malaise, anorexia, myalgia and headache and followed by fever, chills and cough that is non productive or yields small amount of mucopurulent sputum. Diarrhea, pleuritic chest pain, dyspnoea, and confusion or delirium is common.

Klebsiella pneumonia is uncommon typically occurs in middle aged or elderly. The illness begins abruptly with fever, rigors, productive cough, dyspnea, sputum may be tenacious and bloody usually involves the upper lobes.

Staphylococcus aureus is uncommon, onset is generally abrupt and the course rapid, with fever, multiple rigors, purulent sputum production, and pleuritic chest pain.

Chlamydia pneumonia is common in young to middle aged. Occur in large-scale epidemics or sporadics, often mild, self-limiting, and associated with sinusitis, pharyngitis, laryngitis.

Mycoplasma pneumoniae is common in children and young adults, insidious onset, headache, systemic features; often few signs in chest, Erythema nodosum, myocarditis, pericarditis, meningoencephalitis, rash, hemolytic anaemia are seen.

Definition of severe pneumonia:

A British Thoracic Society's definition[10]:

    a) Confusion.

    b) Urea: > 7 mmol /L

    c) Respiratory rate. >30/min.

    d) Blood pressure: Diastolic < 60 mm Hg,

        Systolic < 90 mm Hg.

    e) Age more than 65

American Thoracic Society's definition[13]:

Minor Criteria:

    1. Respiratory rate > 30/min.

    2. Severe respiratory failure (Pao2/FIO2 <250).

    3. Bilateral involvement in chest radiograph.

    4. Involvement of > 2 lobes in chest radiograph (multilobular involvement)

    5. Systolic blood pressure < 90 mm Hg.

    6. Diastolic blood pressure < 60 mm Hg.

Major criteria:

    1. Requirement of mechanical ventilation.

    2. Increase in the size of infiltrates by > 50% in the presence of clinical non-response to treatment or deterioration.

    3. Requirement of vasopressors >4 hours (severe sepsis or septic shock)

4. Serum creatinine > 2mg/dl or increase of > 2mg/dl in a patient with previous renal disease or acute renal failure requiring dialysis.

Selected complications of pneumonia[9]:

1. Complicated pleural effusion: About 40% of patients. Hospitalized with pneumonia have this complication.

2. Lung abscess: These are currently uncommon, with an incidence of 4.5 cases 710,000 hospital admission with pneumonia

3. Recurrent pneumonia of patients admitted to the hospital for the treatment of CAP 10-15% has another episode within 2 years.

Investigations:

In general initial microbiologic studies continue to be ordered routinely by practitioners caring for patients admitted with pneumonia, even though the utility of these initial MBS's in the management of pneumonia remains unclear. Extensive diagnostic testing yields a specific microbiologic etiology in less than 50% of cases.[43]

1. Non invasive methods:

Sputum Gram Stain: Gram Stain was originally devised by the histologist Christian Gram (1884) as a method of staining bacteria in tissues. Gram stain can provide specific diagnostic information and serve as an early guide to therapy. A specimen with fewer than 10 squamous epithelia cells and more than 25 neutrophils per low power field and evidence of predominant bacterial monotype when examined under high power is an accurate indicator of the cause of pneumonia.[44]

The staining technique consists of four steps[17]

1. Primary staining with a pararosaniline dye such as crystal violet, methyl violet or gentian violet.

2. Application of a dilute solution of iodine.

3. Decolouration with an organic solvent such as ethanol, acetone, aniline.

4. Counter staining with a dye of contrasting colour Such as carbal Fuchsin, sofranine or neutral red

The high specificity of a prepondarance of gram positive diplococci on sputum gram stain for the diagnosis of pneumococcal pneumonia has been confirmed. The sensitivity of sputum gram stains for the diagnosis of pneumococcal has varied widely but generally found to be superior to sputum culture.[47]

Limitations of sputum gram stain as a diagnostic tool has been described;

1. Most patients with CAP will not produce a diagnostic specimen that meets Strict standard for interpretation[18]

2. Sputum gram stains are subject to misinterpretation, particularly by inexperienced observers. Tend to misidentify any gram positive cocci as pneumococci, and often overlook H. infleunzae and other gram negative rods.[48] Etiological diagnosis was considered presumptive when a predominant micro organism was isolated from a purulent sample (presence of >25 PMNs and < 10 squamous cells per low magnification field x 10 with compactable Gram staining. Prospective study showed sputum staining to be highly sensitive for Gram negative organisms causing pneumonia and highly specific for diagnosis of pneumococcal.

H Influenza pneumonia. Also it is useful in guiding pathogens oriented antimicrobial therapy.

Sputum culture:

Sputum culture can be a sensitive means for identifying a bacterial cause of CAP when a deep specimen is collected before the initiation of antibiotic therapy, microscopically screened for salivary contamination, and carefully processed for respiratory pathogens.Specimens that are heavily contaminated with saliva or lacking in microscopic purulence are unlikely to provide, useful diagnostic information and may be misleading if potential pathogens are present in the oropharyngeal flora.

The use of specialized media is necessary to culture fastidious organisms such as H. influenza, legionella spp. mycoplasma pneumoniae, mycobacteria. Tissue culture techniques are required to isolate mycoplasma pneumoniae. Even a single dose of an antibiotic agent can suppress bacterial growth from cultural sputum.

A positive sputum culture is the test most relied upon for the diagnosis of pneumonia, but should not be interpreted independently of Gram staining unless an organism is isolated that is not a potential resident of oropharynx, such as legionella pneumophilia, mycobacterium tuberculosis.

The sensitivity and specificity of sputum culture are improved by microscopic screening of each specimen using gram stain. The sputum Gram stain is valuable in guiding the processing and interpretation of sputum culture.

Blood Culture:

Blood cultures are positive in 4% to 18% of patients hospitalized with pneumonia. The relatively low yield of blood cultures and the potentially confounding problem, question the wisdom of routinely culturing the blood in patients with pneumonia. Streptococcus pneumoniae was the most common bacteria found in bacteraemic Pneumonia. Mild to moderate pneumonia, blood culture had a low yield and no impact on management, while the yield of blood cultures is higher in patients with more severe pneumonia. The yield of blood cultures is strongly influenced by prior antibiotic therapy cultures a positive in fewer than 5% of patients who have received antibiotics before the specimen is drawn.

Serological tests:

The usual serological tests involve the measurement of complement fixing antibody levels in the blood. The complement fixation test is seldom of immediate value and when positive usually provide diagnostic information retrospectively as two paired samples are required in order to demonstrate a four fold rise in the titer of specific antibodies.

It is usual to wait about 14 days between the two samples, although in some infections, such as mycoplasma, a rise may be detected earlier, in others notably legionella, the rise may take several weeks.

Newer microbiological technologies[22]:

DNA probes have been developed for characterizing target organisms and minute amount of target DNA can be amplified by the polymerase chain reaction (PCR). A PCR

assay has recently been tested on the serum of patients with bacteraemic pneumococcal pneumonia and was found to have a sensitivity of 100% and specificity of 94%. Similar probes have been or are being developed for a wide range of organisms including Legionella pneumophila, Mycoplasma pneumoniae, Nisseria meningitidis, and Mycobacterium tuberculosis.[16]

Roentegenographic findings[23]:

An abnormal chest x-ray is a sine a qua-non in pneumonia providing an immediate visual impression of extent of involvement and it is the integration of the information obtained from the clinical examination and the roentgenogam which often provides the key to diagnosis.

It may be pointed out that the lung differs from all other organs in being able to hide nothing of its structure from the roentgenologist, who regards it as a window through which he may look into the body in search of the disease. It is indeed a delicate mirror reflecting the gross changes of a pneumonic process.

The radiological appearances of acute inflammation of the lung are very variable and the picture presented is always one of an increase in the size and number of lung markings, or of consolidation, or of both[19]. There was no relation between hydration status of the patient and radiographic appearance as was thought previously[20].Pneumonias tend to conform to one of three pathological and roentgenographic patterns.

1. Alveolar or air space pneumonia

2. Broncho-pneumonia

3. Interstitial pneumonia.

In airspace pneumonia the organism causes an inflammatory exudate that spreads from the one alveolus to the next via the communicating channels, the pores of Kohn, and the canals of Lambert Segmental boundaries are not preserved, and the bronchi, relatively uninvolved remain patent.

The roentgenographic results are non-segmental consolidation with air bronchograms, the classic example being pneumococcal pneumonia. Some organisms produce bronchopneumonia, which consists of inflammation in the conducting airways, especially terminal and respiratory bronchioles, and the surrounding alveoli.

Because interalveolar spread in the peripheral air spaces is minimal, the pneumonia tends to maintain a distribution corresponding to the involved pulmonary segment. Inflammation affects the bronchi themselves, sometimes causing atelectasis, and air bronchograms are absent. An example is staphylococcal pneumonia.

The microbial etiology of pneumonia cannot be accurately predicted by its roentgenographic characteristics. The clinician can at best make an informed guess about likely causative organisms as so much overlap occurs on pattern of appearance[3].

Nevertheless, certain appearances are more typical of some organisms than others and two such merit discussions in adults, staphylococcal pneumonia may some times be recognized when it presents with multiple rounded areas of consolidation, which often cavitate in children, staphylococcal pneumonia may result in large tension air cysts or pneumatocoeles, but these are rarely found in adults.

Round pneumonia, a form commonly found in children occasionally found in adults caused by Strep pneumonia appearing as small dense nodule to large ill defined oval opacity[20]. The other pneumonia which may some times be recognized from the radiograph is the Friedlander's pneumonia which commonly presents with areas of consolidation, which are commonly dense and homogenous and may be unilateral or bilateral. Cavitation is common. The recognizable feature, which is not seen in every case, is a swelling of the affected parts of the lung producing a bulging of the fissures and displacement of the landmarks. A similar appearance may be seen, on occasions, in other kinds of pneumonia when they are breaking down and cavitating, but with Friedlander's pneumonia enlargement of the lung takes place before recognizable caviation occurs[19].

Enlarged hilar and mediastinal glands are not a feature of primary pneumonia though it is said that the hilar shadows are prominent in a few cases of virus pneumonia, in infectious mononucleosis, and occasionally in pneumonia in children.

It is an important working rule that cases showing consolidation and definite enlargement of the hilar or mediastinal glands are not cases of primary pneumonia but usually suggest secondary pneumonia (neoplasm). Inter observer reliability of chest radiograph has important implication on the pattern recognition and hence the identification of causative organism.

A study by Michael N Albaum et al on 282 patients with signs of CAP showed that, radiologist identified the presence of infiltrate, multilobar disease and PE with fair to good interobserver reliability. However interobserver reliability for the pattern of infiltrate and presence of air bronchogram was poor[21].

Radiographic response to treatment lags well behind clinical improvement. In elderly patients resolution may take much longer, and occasionally a primary pneumonia, with no complication, may persist for up to 6 months before resolving completely.

In a few cases the consolidation and breakdown forming a lung abscess. Non-resolution usually suggests a secondary pneumonia with an underlying reason like bronchogenic carcinoma, foreign body, bronchiectasis etc. Thus a roentgenographic examination of the lungs serves two major roles. It permits detection of pulmonary involvement in an ill patient and, far more frequently, the rontegenogram having detected the potential disease provides a guide to the selection of subsequent diagnostic and therapeutic procedures[22].

The different patterns of radiological presentation are[23]:

1. Lobar or segmental consolidation.
2. Non homogenenous infiltrates.
3. Cavity infiltrates.

Factors that impact negatively on pneumonia resolution include advanced age and presence of serious co morbid illness such as diabetes mellitus, renal disease, COPD or alcoholism[24].

Recent data demonstrate that radiographic clearing (resolution) of pneumonia is most influenced by number of lobes involved and age of patient. Radiographic clearance of pneumonia decreases by 20% per decade after the age of 20 and patients with multilobar infiltrate take longer to clear than those with unilobar disease[24].

II. Invasive methods:

Thoracocentesis[3]: Thoracocentesis should be performed to exclude empyema whenever a pleural effusion is readily evident on the chest radiograph of patient with CAP.

Transtracheal aspiration:

In patients with pneumonia Gram stain of TAS provides a prompt and accurate bacteriologic diagnosis in more than 90% of pneumonia cases. The rate of isolating of microorganisms by culture of TAS is reported to be between 43 and 47%[25].

Transthoracic Needle Aspiration:

Patients in whom pneumonia is suspected and where transthoracic needle aspiration is indicated (immuno-compromised, nosocomial, serious CAP caused by uncommon pathogen or that fails to respond to appropriate empirical treatment), this should be performed prior to antibiotic therapy, in those patients in whom the infiltrate is smaller than a lobe Fluoroscopic control is advisable, and it would also be advisable so that a trained physician carry out the test. Pneumothorax was most common complications (18%) hemoptysis complicates 3% [26].

Other Laboratory Findings:

The white cell count is frequently raised in bacterial pneumonia, with a neutrophilia. Elderly patients are not always able to mount such a response. Sometimes when sepsis is overwhelming there may be leucopenia.

Lymphocytosis may occur in infections with atypical organisms such as chlamydia, coxiella or mycoplasma. Other biochemical abnormalities have been noted, such as raised urea, bilirubin, transamiriases and alkaline phosphatase,

hypophosphataemia and hyponatraemia. Urinalysis may detect small amounts of protein and both red and white cells may be seen on microscopy.

Pneumonia severity index (PSI)[27]:

Severity of illness scoring system based on pneumonia patient outcome research team (PORT)**.**

Patient characteristic no. of points

Age

Men Age, years

Women Age, years -10

Nursing home residents Age, years + 10

Coexisting illness

Neoplastic disease 30

Liver disease 20

Congestive cardiac failure 10

Cerebrovascular disease 10

Renal disease 10

Physical examination findings

Altered mental status 20

Respiratory rate >30/min 20

Systolic blood pressure < 90 mm of hg 20

Temperature <35c or > 40c 15

Pulse rate >125/min 10

Laboratory and Radiographic findings

Arterial PH < 7.35 30

Blood Urea Nitrogen> 30mg/dl 20

Sodium <130 mmol/l 20

Glucose >250 mg/dl 10

Hematocrit <30% 10

Partial pressure of arterial oxygen < 60mmHg 10 Pleural effusion 10.

Risk classification and relation with mortality

Risk class criteria :

  I.   Age < 50yrs, no existing illnesses, vital signs

        abnormalities, < 70 points

 II.   70 points

III.   71 – 90 points

IV.   91 – 130 points

 V.   131 points

Treatment:

Treatment includes general and antimicrobial (empirical and specific). Since the etiology of pneumonia is frequently unknown, initial antibiotic therapy is often empirical. The initial choice of antibiotic regimen should be influenced by:

Whether the infection is judged to be severe or not;

  1. The Presence of co morbid disease

  2. The patients age

3. Antimicrobial already received in the community.

The possible consequences of missing the responsible pathogen in a very ill patient is obvious and cover must therefore be broad.

The presence of certain co morbidities will focus the physician's attention on the increased probability of particular organisms or groups of organisms eg., are those associated with overt oropharyngeal aspiration, with immunosuppression.

When the patient has chronic lung disease such as emphysema, chronic bronchitis or bronchiectasis, the initial choice of antibiotic may also be influenced by knowledge of likely colonists such as H.influenzae or of previous microbial isolates such as Moraxella catarrhalis or P aeuroginosa, in earlier infective exacerbations.

With increasing prevalence of beta-lactamase producing pathogens and the development of other forms of resistance. Some knowledge of local patterns of microbial susceptibility to those antibiotics in common use is helpful.

Treatment of selected pneumonias[28]:

Organisms Antimicrobial therapy

Streptococcus pneumonia penicillin G, amoxicillin and alternatives like Macrolides, cephalosporins, Doxycycline, fluroquinolones, clindamycin, vancomycin. Hemophilus influenzae Cefotaxime, ceftriaxone, cefuroxime, doxycyclin, azithromycin, TMP-SMZ. Staphylococcus aureus for methicillin – susceptible strains: a penicillinase resistant penicillin with or with out rifampin or gentamycin and alternatives like cephalosporins, clindamycin, TMP-SMZ, vancomycin For methicillin resistant strains: vancomycin with or with out gentamycin or rifampin.

Klebsiella pneumonia Third generation cephalosporins, for severe infection add an aminoglycoside and alternatives like aztreonam, imipenem, beta- lactum/ beta- lactamase or fluroquinolones.

Escherichia coli Third genatration cephalosporin, for severe infection add an aminioglycoside and alternatives like aztreonam, imipenem, beta- lactum/ beta- lactamase . inhibitor or fluoroquinolones.

Pseudomonas aeuroginosa Antipseudomonal beta-lactam plus an aminiglycoside. Alternatives like ciprofloxacin plus an aminoglycoside or an antipseudomonal beta lactam.

Anaerobes Clindamycin, beta- lactum/ beta- lactamase inhibitor, imipenem. Mycoplasma pneumoniae Doxycycline or erythromycin. Alternatives like clarithromycin, azoithromycin or fluoroqunolones.

Legionella species Macrolide with or without rifampin, a fluoroquinolone and alternatives like doxycycline with or without rifampin.

C-reactive protein:

C – reactive protein was discovered by Tillet and Francis in 1930 [29]. they were investigating serological reactions in pneumonia with various extracts of penumococci and observed that a non type specific somatic polysaccharide fraction, which they designated fraction C, was precipitated by the sera of acutely ill patients. After the crisis, the capacity of the patients sera to precipitate C polysaccharide (CPS) rapidly disappeared and the C-reactive material was not found in sera from normal healthy individuals.

Avery and his collaborators characterized the C-reactive material as a protein which required calcium ions for its reaction with CPS and introduced the term "acute phase" to refer to serum from patients acutely ill with infectious disease and containing the C-reactive protein [30,31]

Lofstrom independently described a non-specific capsular swelling reaction of some strains of pneumococci when mixed with acute phase sera and subsequently showed that the substance responsible was CRP[32]. He detected CRP in non-infectious as well as infectious conditions; and the acute phase reaction, in which the concentration of certain plasma proteins increases is now recognized as a general and non-specific response to most forms of infective and non-infective inflammatory processes, cellular and / or tissue necrosis and malignant neoplasia

A feature of most forms of inflammation, infection and tissue damage is the increase in the circulating concentrations of various plasma proteins known as acute phase reactants[33]. These reactants are mainly produced by hepatocytes and the increased expression of acute phase protein genes is driven by cytokines, which are produced by activated macrophages and other cells. During inflammation the plasma concentration of CRP can rise upto 10000 fold[34]. The plasma concentration of CRP is determined only by its production rate; which provided liver function is normal depends on the concentration of cytokines and other mediators that reach the hepatocytes. Concentration of CRP is directly correlated with the presence and severity of coronary, cerebral and peripheral atherosclerosis.

Synthesis, Structure and Binding properties of C – reactive protein:

CRP is synthesized by hepatocytes[35] and is normally present as a trace constituent of the plasma.

The median circulating concentrations of C – reactive protein is 0.8 mg/dL. Normal range may be as low as 0.07 mg/dl and among apparently healthy individuals 90% have less than 3 mg/dl and 99% have less than 10 mg/dl[36].

The rate of CRP synthesis and secretion increases within hours of an acute injury or the onset of inflammation[37], probably under the influence of humoral mediators such as leucocyte endogenous mediator (endogenous pyrogen)[38] and prostaglandin PGE. The serum CRP concentration may reach peak levels as much as 300 µg/ml within 24-48 hours. CRP belongs to the pentroxin family of proteins with a molecular weight of 1,05,500.

It consists of five, identical non-glycosylated polypeptide subunits, which are noncovalently associated in a disc like configuration with cyclic pentameric symmetry[39]. This arrangement and the amino acid sequence of the subunit are distinct from all other known proteins, with the exception of serum amyloid P component[40].

In addition to the reaction with the pneumococcal C- Polysaccharide by which it was discovered, CRP also undergoes calcium dependent binding to choline phosphatides such as lecithin, lysolecithin and sphingomyelin to some other lipids which do not contain phospharyl choline (PC) to PC-containing and non-PC containing microbial polysaccharides and peptidopolysaccharides, which are present in diverse bacteria, fungi and parasites and to poly anions including nucleic acids, heparin and dextran sulphate.

Although CRP does bind materials lacking PC, free PC is the best inhibitor of all these reactions and is itself bound by CRP with very high affinity ($Km-10^{-7}m$). In addition CRP binds in the absence of calcium Ions to poly cations, including histones, leucocyte cationic protein, myelin basic protein and protamine. The binding site for poly cations seems to be distinct from the calcium dependent site for PC but the two sites interact[41,42].

Functional properties of C – reactive protein:

CRP precipitates soluble ligand and agglutinates particulate ligands[42,43]. Once complexed via either its calcium dependent or its polycations binding sites, it becomes a potent activator of the classical complement pathway starting C_1q.

Complement activation proceeds as efficiently as with IgG antibody and leads to fixation of C_4b and C_3b, which can mediate the important complement dependent adherence reactions and to fixation of the terminal complex C_5b-C_9, causing lysis if the ligand is on a cell surface. Complement split fragments, active in the fluid phase, are also generated. CRP like antibodies can thus bind to ligands, opsonise materials for phagocytosis and initiate cell damaging and inflammatory reactions.

Other activities which have been ascribed to CRP include:

Selective binding to T-lymphocytes and modification of some of their functions[44]. Suppression of platelet aggregation and activation reactions[45].
Enhancement of the activity and motility of phagocytic cells.

However, none of these observations have proved reproducible with highly purified CRP, either in the laboratories, which originally reported them or elsewhere[46]. CRP

complexed in a suitable way may bind to lymphocyte bracing FC(y) receptors (including B, T and non-B, non-T cells) both in vivo and in vitro, but the functional significance of this is not known[47,48].

The role of C-reactive protein in Vivo:

The role of C – reactive protein in vivo is not known although under some circumstances it can cause inflammation. For example, intracutaneous injections of CPS in acutely ill patients elicits a characteristic immediate Wheal and Flare reaction, followed by a more extensive edematous erythema which is maximal at 6-10 hours. Local deposition of CRP may contribute to the chronicity of the lesions of cutaneous vasculitis[49].

The complement mediated hemolysis, which sometimes follows the bite of the brown recluse spider (Loxosceles recluse) depends on CRP.

Whereas CRP may play a part in the pathogenesis of the many inflammatory conditions, in which its circulating concentration is elevated. It seems unlike that this is its major role or that it has been conserved in evolution for this reason. Probably the normal function of CRP is generally beneficial to the organisms as a whole and this may be acting as an easily broad spectrum recognition mechanism for the products of pathogenic microorganisms.

On the other hand increased CRP production is a feature of non infective as well as infective disease and CRP binds to a wide range of autogenous products. Lipids and

phospholipids, polycations and poly anions all of which are constituents of cells and likely to be abnormally exposed in or released from damaged tissues.

In Vivo binding of CRP to necrotic cells has been described and contribute to resolution and repair. However, the main role of CRP, for which it evolved and has been conserved is to recognize in the plasma the potentially toxic autogenous materials released from damaged tissues to bind them and thereby to detoxify them and / or facilitate their clearance[50].

Clinical Applications of Measurements of Serum C-reactive Protein:

The C-reactive protein response is non-specific and can therefore never be precisely diagnostic but there are important differential patterns in certain diseases. Also C-reactive protein production per se is not suppressed or modified by any drugs or other therapies currently in use unless these effect the underlying pathological process, which has provoked the acute phase reaction.

The only condition which interferes with normal C-reactive protein response is severe hepatocellular impairment. C – reactive protein levels thus usually provide an objective index of the presence and activity of disease of response to treatment. By virtue of its speed and extended dynamic range, the C-reactive protein response yields valuable information, which when interpreted at the bedside together with all other available clinical and laboratory results can contribute significantly to management of wide range of conditions[36].

It can be used for: The Acute phase C-reactive protein (CRP) is synthesized in the liver in response to inflammatory cytokines and may increase 1000 folds during an acute

phase response. Because of its short half life of 19 hours. CRP levels can be expected to fall quickly after efficient elimination of the microbial stimulus. Thus CRP may sufficiently reflect the individual balance between the microbes and the immune system

Screening for organic disease: CRP production is a very sensitive index of organic disease and raised CRP is unequivocal evidence of active disease.

Monitoring the extent and activity of disease: Serial measurements reflects activity and response to treatment and can be used for monitoring.

Detection and management of Intercurrent Infection:

A raised level is a useful guide to the possible presence of infection in otherwise normal subjects or individuals with primary condition, which predisposes to infection. Effective antimicrobial therapy of infection is always associated with a prompt fall in CRP while persistent CRP elevation indicates continuing infection and /or activity of the underlying disease. There is no other objective test which yields this sort of information so accurately and changes in results of clinical examination and tests of organ function usually lag hours or days behind the C-reactive protein response[36].

Conditions associated with major elevation of C-reactive protein:

Allergic complicationErythema nodosum leprosum, of infection   Rheumatic   fever Inflammatory disease Rheumatoid   arthritis,   juvenile   Chronic   arthritis,   systemic vasculitis, polymyalgia, rheumatica, ankylosing   spondylitis,   psoriatic   arthritis, Reiter's disease, Crohn's disease, Familial   Mediterranean fever. Allograft rejection, Renal transplantation,

Malignant neoplasia, Lymphoma, Sarcoma, Myocardial infarction, Tumor embolization, Acute Pancreatitis, Trauma, Surgery, Burns, Fractures[36].

Conditions associated with minor elevation of C-reactive Protein:

1. SLE

2. Systemic sclerosis

3. Dermatomyositis

4. Ulcerative colitis

5. Leukemia

6. Graft versus host disease[36]

Studies have shown that elevated CRP in community acquired pneumonia is independently associated with requirement for inpatient care, that higher CRP levels results in longer duration of hospital stay and poorer clinical outcome. One of the major advantage of CRP is that serial measurements can be taken as a marker of treatment response. In patients admitted to hospital, a CRP level that falls by 50% or more in 4 days indicates a low risk of 30 day mortality, need for ventilation and/or inotropic support, or development of complicated pneumonia[52].

CRP <100mg/L provides a high negative predictive value comparable with CURB65 [New onset of confusion, Urea > 7 mmol/L, respiratory rate more than or equal to 30 breaths/min, systolic blood pressure <90 mm Hg or diastolic blood pressure less than or equal to 60 mm Hg and age more than or equal to 65 years] and pneumonia severity index rules[52].

Luis Coelho et al[50] , in their study concluded that daily CRP measurement after antibiotic prescription is useful in identification of severe community acquired pneumonia as early as day 3, in patients with poor outcome. The identification of CRP pattern of response to antibiotic therapy was useful in the recognition of the individual clinical course,either improving or worsening, as well as rate of improvement.

Jordi Almirall et al[51], in their study concluded that , serum CRP level is a useful marker for establishing the diagnosis and prognosis of CAP . High CRP values are suggestive of severity, which may be value in deciding about the appropriateness of inpatient care.

Robin P. Smith Mb et al[52], in their study concluded that, CRP is a sensitive marker of pneumonia. A persistently high or rising CRP level suggests antibiotic failure or the development of an infective complication.

James D. Chalmers et al[53], in their study concluded that, admission CRP<100 mg/l has reduced risk for 30-day mortality, need for mechanical ventilation and /or inotropic support, and complicated pneumonia. Failure of CRP to fall by 50% or more at day 4 leads to increased risk of 30-day mortality, need for mechanical ventilation and/or inotropic support, and complicated pneumonia.

E. García Vázquez et al[53], Two different uses of CRP have been investigated. Firstly, as a diagnostic tool to distinguish between noninfectious and infectious conditions and within the latter between viral and bacterial or superficial and deep infections , CRP levels are usually lower in viral and superficial bacterial infections than in deep bacterial infections. Secondly, as a prognostic and follow-up test, as serial measurements may be

useful to evaluate the response to antibiotic treatment and to detect complications in patients with infections .

Mandell LA et al[56] .Severity assessment is a crucial component in the management of patients presenting with CAP to guide physicians in clinical decisions. There are large numbers of pneumonia-specific severity and generic sepsis scores available for this purpose. The pneumonia severity index is regarded as the 'gold standard test' but complexity limits its use in routine clinical practice. Given that simplicity is critical to acceptance for general use, CRB65 is the most useful clinical score currently available. Severity assessment tools are evolving, but at present have major limitations and should be used with caution and only in conjunction with clinical judgment.

Chalmers JD, Singanayagam A[57], Admission CRP <100 mg/L has reduced risk for 30-day mortality, need for mechanical ventilation and/or inotropic support, and complicated pneumonia. Failure of CRP to fall by 50% or more at day 4 leads to an increased risk for 30-day mortality, need for mechanical ventilation and/or inotropic support, and complicated pneumonia. C-reactive protein is an independent marker of severity in community-acquired pneumonia.

Barlow GD, Nathwani D[58], CURB65 should not be supplanted by SIRS or SEWS for initial prognostic assessment in CAP. Further research to identify better generic prognostic tools is required.
The CURB65 pneumonia severity score outperforms generic sepsis scores and early warning in predicting mortality in community acquired pneumonia.

R Menéndez et al[60] , Biological markers as an expression of systemic inflammation have been recognised as useful for evaluating the host response in community-acquired pneumonia (CAP).

Low levels of CRP and PCT at 72 h in addition to clinical criteria might improve the prediction of absence of severe complications.

James D Chalmers,Aran Singanayaga et al[61] ,The PSI, CURB65 and CRB65 scores all predicted 30 day mortality with moderate to good accuracy.There were no significant differences in overall test performance between these scores, suggesting that clinicians may choose the scoring system best suited to their local needs. Although overall test accuracy was similar, there were some differences in the performance characteristics between the scores. The low negative likelihood ratio suggests that PSI may be superior at identifying low risk patients, while a higher positive predictive value suggests that CURB65/CRB65 may be superior for identifying high risk patients.The clinical importance of these differences is, however, difficult to establish.

Buenos Aires, Argentina,Luna et al[63] , Besides the usefulness as a diagnostic tool for pneumonia, etiologic diagnosis, and outcome marker, there could be some place for CRP in the follow-up of pneumonia. Ninety-nine percent of healthy young adults have a median CRP concentration of < 10 mg/L.Following an acute-phase stimulus, values may increase 10,000-fold. Synthesis starts very rapidly after a single stimulus, serum concentrations rising > 5 mg/L by approximately 6 h and peaking at approximately 48 h. The plasma half-life of CRP is approximately 19 h and is constant under all conditions of health and disease, so that the sole determinant of circulating CRP concentration is the synthesis rate.When the stimulus for increased production completely ceases, the circulating CRP concentration falls rapidly, at almost the rate of plasma CRP clearance. These characteristics of quick rise and decrease make this parameter an interesting one in the measurement of the evolution on pneumonia that could be used together with other

tools in the evaluation of response to therapy and prediction of outcome. Recently, Lauritzen et al, in an experimental model of porcine bacterial pneumonia, demonstrated that clinical evidences of infection became apparent 20 h after inoculation. Plasma CRP and IL-6 increased; then, in an antibiotic-treated group of animals, CRP and IL-6 reverted significantly toward normalization within 24 h, while this did not happen in those animals not receiving antibiotics..

The initial selection of an adequate empirical therapy and the evaluation of the response to therapy are two issues that are highly related to outcome of severe community-acquired and hospital-acquired pneumonia. CRP levels may help evaluate patient management and response to antibiotic therapy.

Fig No:1 Right lower and middle lobe pneumonia

Fig No:2 Right lower lobe pneumonia

Fig No:3 Right middle lobe pneumonia

MATERIALS AND METHODS

Source of data

100 consecutive patients with Community Acquired Pneumonia, admitted to Shri B.M.Patil Medical College Hospital and Research Centre, Bijapur from October 2008 to May 2010 were included.

Sample size:

With incidence of CAP 30% (reference: park spm text book 19 th edition) and level of confidence 95% with 30 % of allowable error the sample size is 99.5= 100.

Using statistical formula:-

$$n = \frac{(1.96)^2 \times p \times q}{L^2}$$

Statistical analysis:

Diagramatic presentation

Mean +/- s.d

Suitable statistical tests- paired "t" test or chi square test...

Materials and methods

Method of collection of data

The study was carried out on patients presenting with community acquired pneumonia.

Inclusion criteria

All patients presenting to hospital with community acquired pneumonia during the study period (Oct 2008 to May 2010) and absence of exclusion criteria.

Exclusion criteria:

Hospital acquired pneumonia

Active thoracic malignancy

Conditions likely to cause diagnostic confusion or where chest radiograph changes are equivocal

Chronic lung disease

Immunosupression

Solid organ malignancy

Hematological malignancy

Chronic liver disease or cirrhosis

Aspiration pneumonia

Methods: Estimation of CRP in serum by immunoturbidimetric method.

Test: Mix 60 microlitre of standards and samples with 1000 micro litre of buffer. Read optical density (OD1) of standards, controls and samples at 340 nm. Add 100 microlitre of CRP antiserum. Mix and incubate for 5 min at room temperature. Read optical density (OD2) of standards, controls and samples at 340 nm.

Calculate OD's, plot a standard curve and read the concentration of controls and samples.

OBSERVATIONS AND RESULTS

Total number of patients included in the study are 100.

Sex wise distribution of patients:

Table no:1

Sex	Number of patients
male	78
female	22

Graph 1
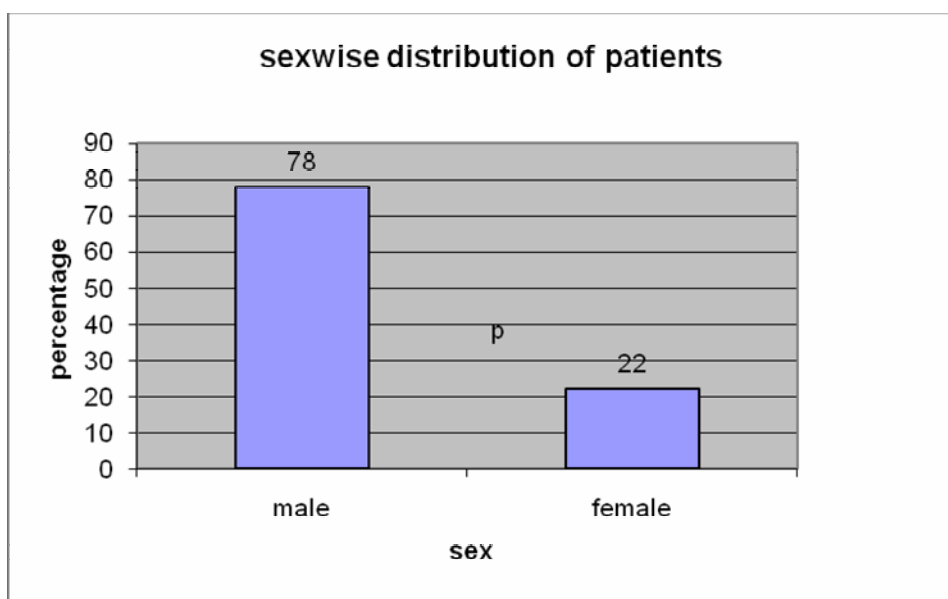
No.   of   males   were   78(78%)   and   females   were   22(22%).

Distribution of patients according to age:

According to age patients were distributed in to nine groups and tabulated as:

Table no:2

Age intervals	Number of patients
16-20	4
21-25	13
26-30	10
31-35	21
36-40	7
41-45	19
46-50	12
51-55	6
56-60	9

Graph 2
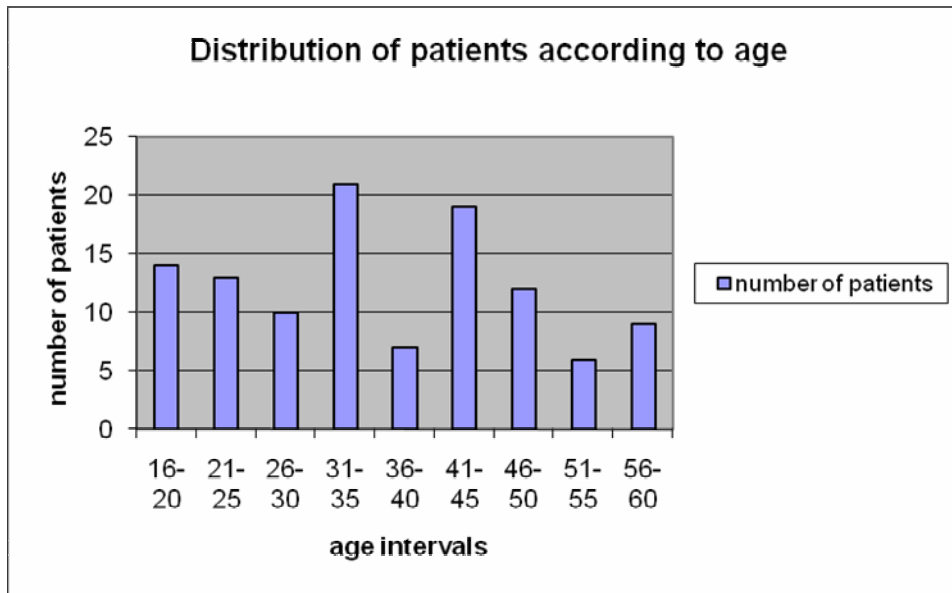
Mean age :38.36 yrs

Distribution of patients according to anatomical diagnosis:

Table no:3

Part of lung involved	Number of patients
RMLP	28
RLLP	23
BEP	19
RMP	14
LULP	6
REP	5
RULP	2
RUMP	1
LLLP	1
LEP	1

Most commonly involved part of lung was combined right middle and lower lobes.

Graph 3

Distribution of patients according to anatomical diagnosis

number of patients

30
25
20
15
10
5
0

□ number of patients

RMLP   RLLP   BEP   RMP   LULP   REP   RULP   RUMP   LLLP   LEP

part of lung involved
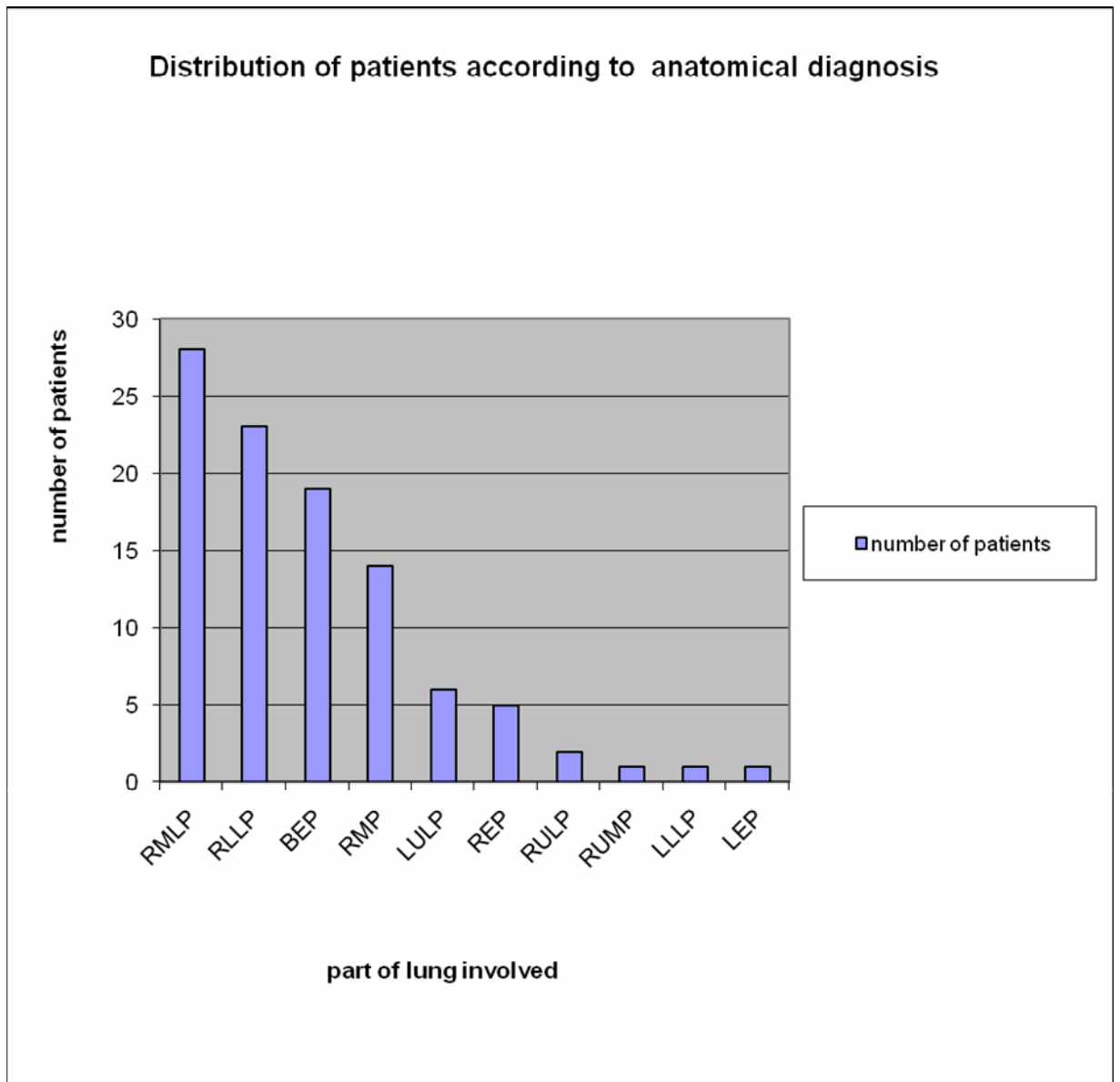
Distribution of patients according to sputum culture and sensitivity:

Table no:4

Sputum culture and sensitivity	Number of patients
Sterile	65
Klebisella	14
Staphylococcus	12
Pneumococcus	5
Streptococcus	4

Graph 4
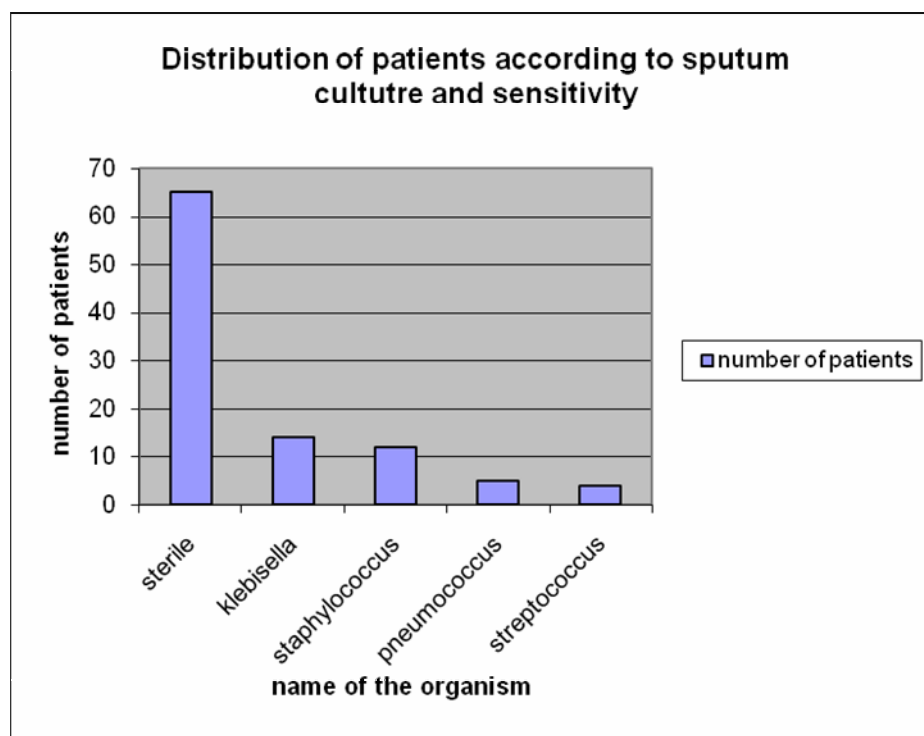
Most common organismm isolated in sputum culture was klebsiella pneumonia.

Distribution of patients depending on comparision of crp levels on day 1 and day 4 after admission:

Table No:5

CRP levels	Number of patients
Increased	30
Decreased	70

Graph 5

CRP-Inference
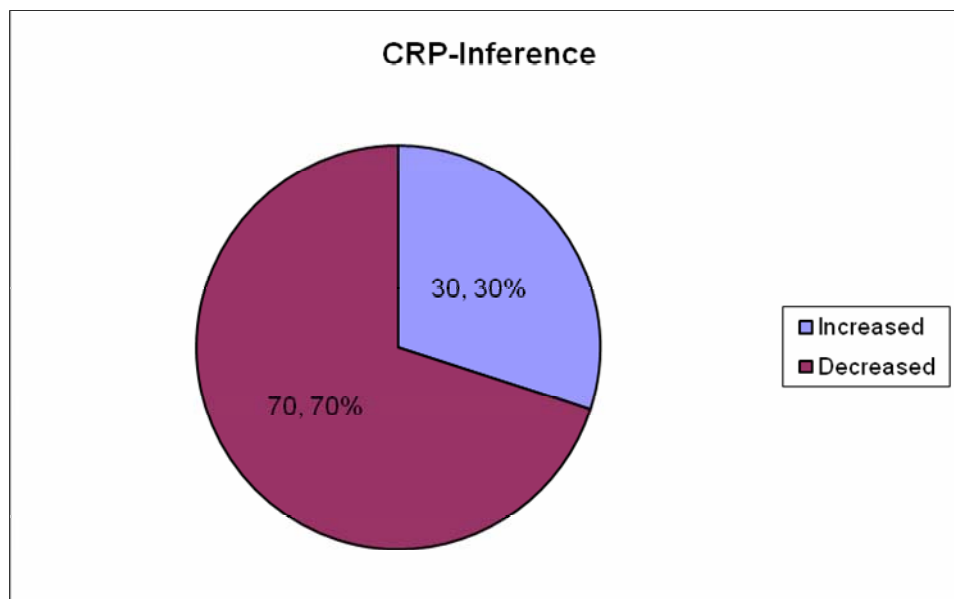
CRP levels were increased in 30(30%) patients on day-4,and decreased in 70(70%) patients,when compared to day -1 CRP levels

Distribution of patients depending on duration of stay in hospital:

Table no:6

Duration of stay (in days)	Five-ten	Eleven-fifteen	Sixteen-twenty
Number of patients	47	44	9

Graph -6
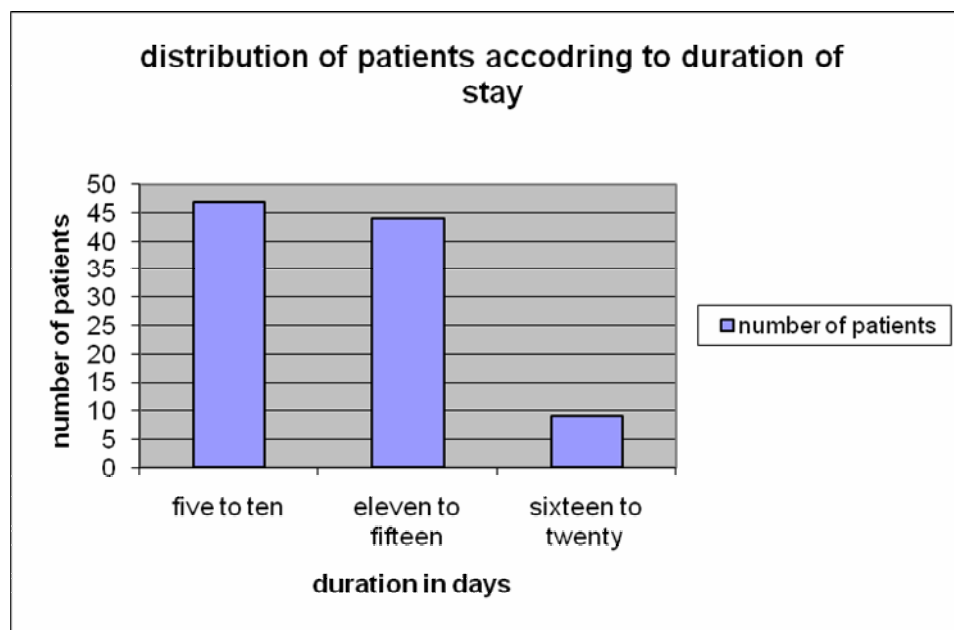
Mean duration of hospital stay:11.86 days

Distribution of patients according to duration of stay in relation to CRP values:

Table -7

	CRP increased	CRP decreased
Five to ten	4	43
Eleven to fifteen	18	26
Sixteen to twenty	8	1

Graph-7
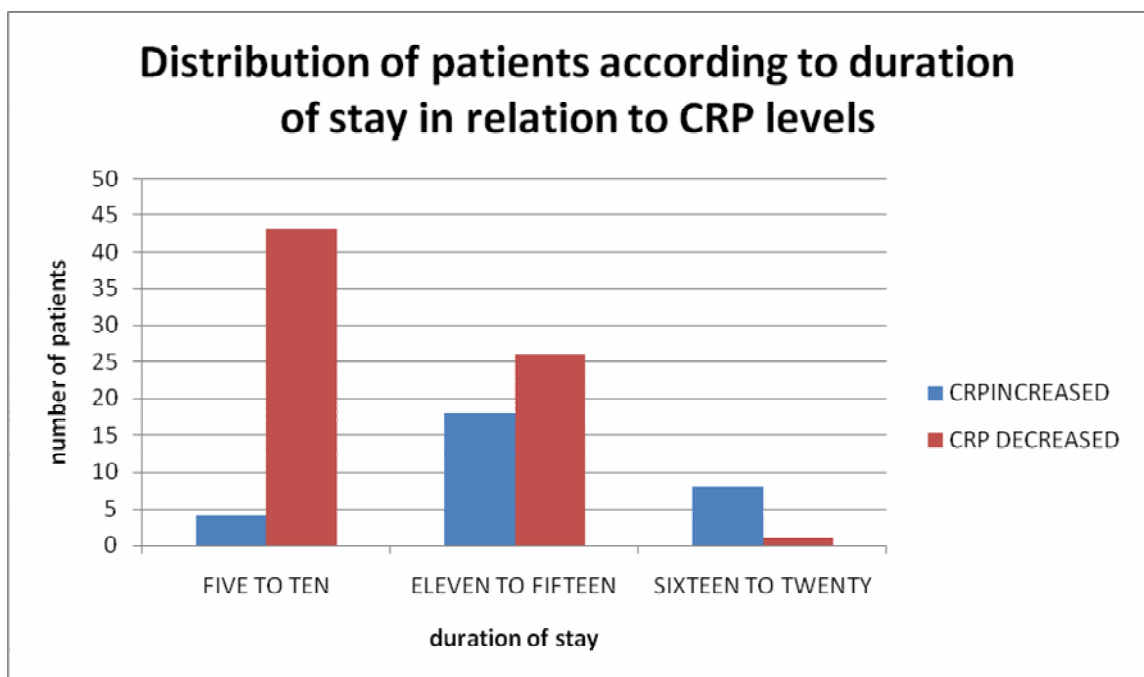
Duration of hospital stay is increased in patients with increased levels of day-4 CRP levels.

Distribution of patients depending on outcome at discharge:

Table no:8

Outcome at discharge	Number of patients
Improved	85
Unchanged	8
Worsened	3
Expired	4

Graph-8
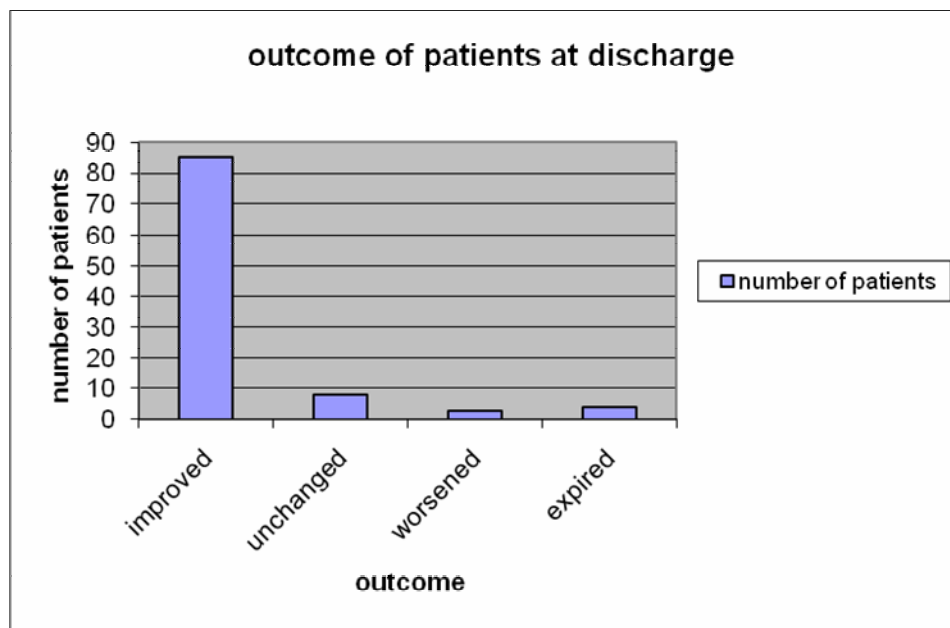
Total number of patients included in study were 100. 85(85%) were improved, 8(8%)were discharged with status of unchanged, 3(3%)were discharged with status of worsened, and 4(4%) were expired.

Distribution of patients according to final out come at end of 30 days after discharge:

Table no:9

Final outcome	Number of patients
Improved	87
Expired	13

Graph- 9

final outcome of the patients at the end of 30 days after discharge
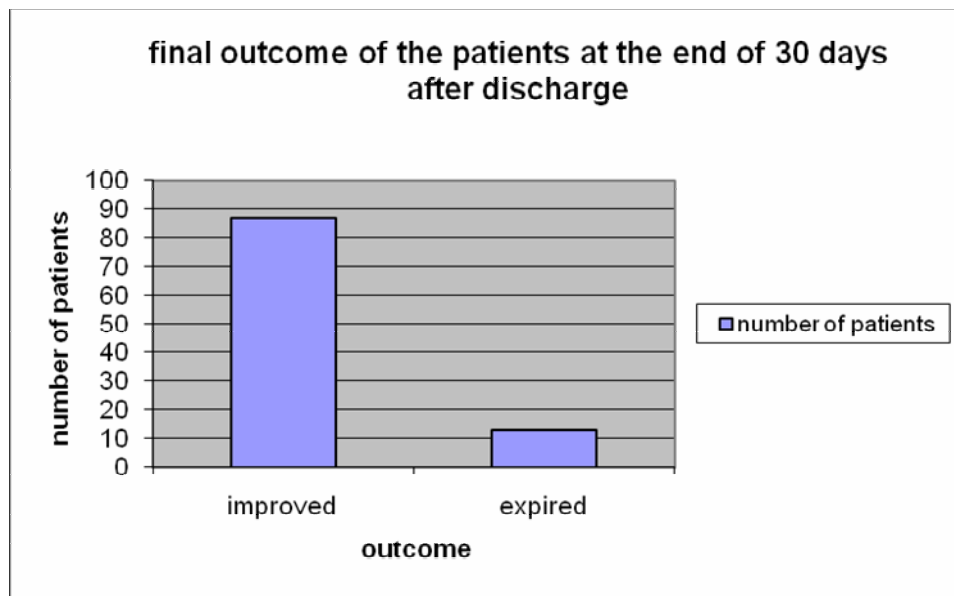
Total number of patients included in the study were 100. 87(87%) were improved and 13(13%)were expired at the end of 30 days after discharge.

Distribution of patients according to antibiotics used:

Table No:10

Antibiotic used	Number of patients
Levo+pip+taz	47
Cef+s+levo	40
Pip+taz+levo+orni	8
Pip+taz+levo+amikacin	3
Pip+taz+amikacin	1
Cef+s+levo	1

Most commonly used combination of antibiotic was levofloxacin with Pipercillin and

Tazobactum.
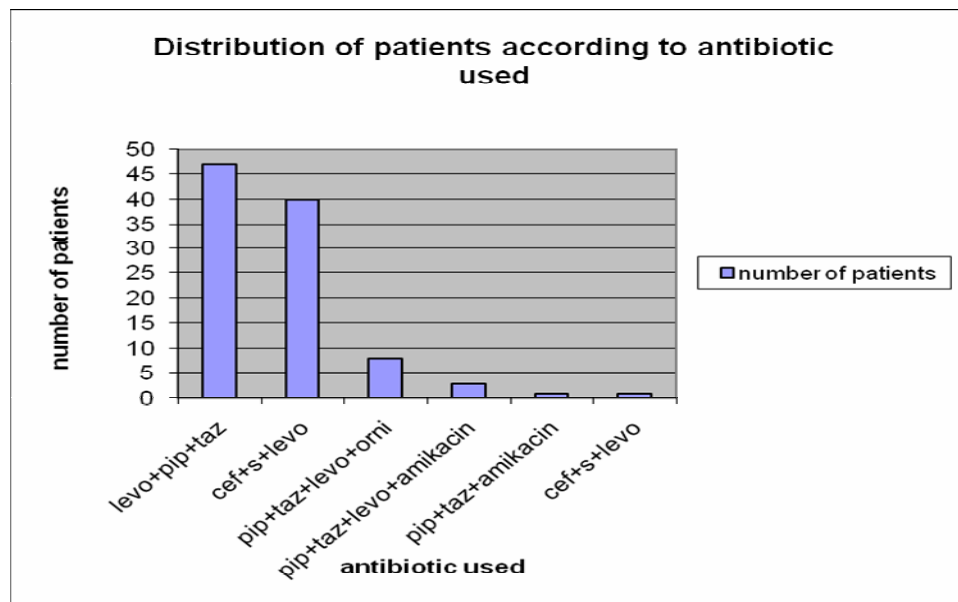
Graph-10

Distribution of patients of according to need for the ventilatory support in both

groups:

Table-11

CRP Level	No of Patients
CRP increased group	4
CRP decreased group	1

Graph-11

Need for ventilatory support in relation to CRP values
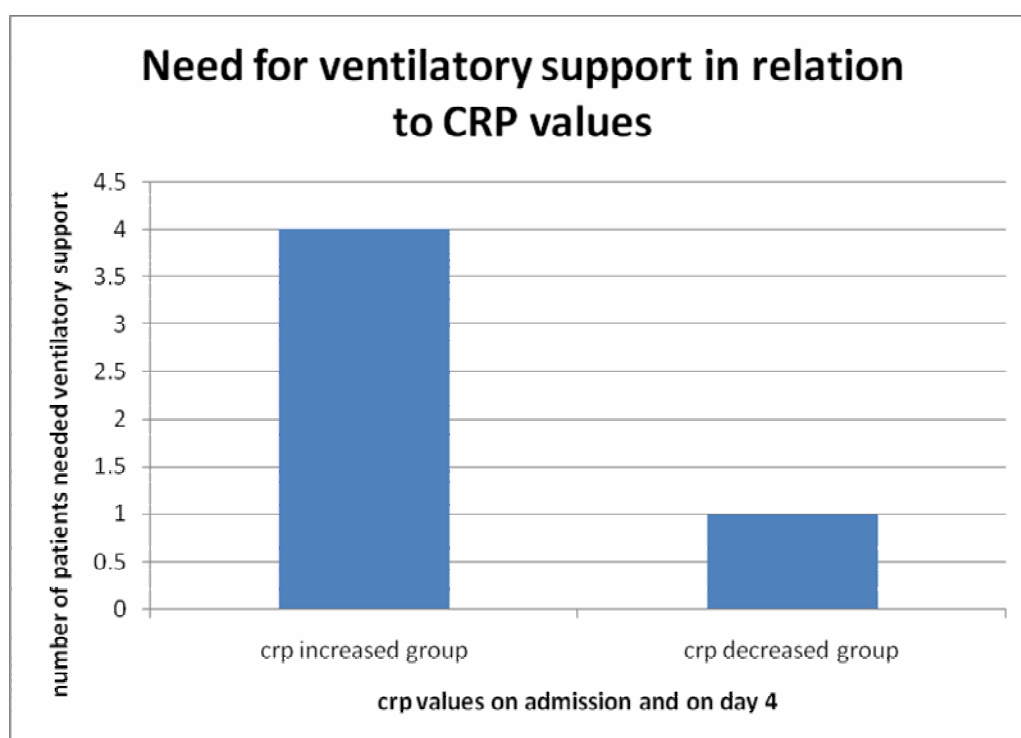
Total number of patients needed ventilator support was 5(5%). 4(80%)were among the group with increased CRP and 1(20%)was among the group with decreased CRP.

Distribution of deaths in patients according to CRP levels:

Table-12

CRP Level	No of Patients
CRP increased	10
CRP decreased	3

Graph-12
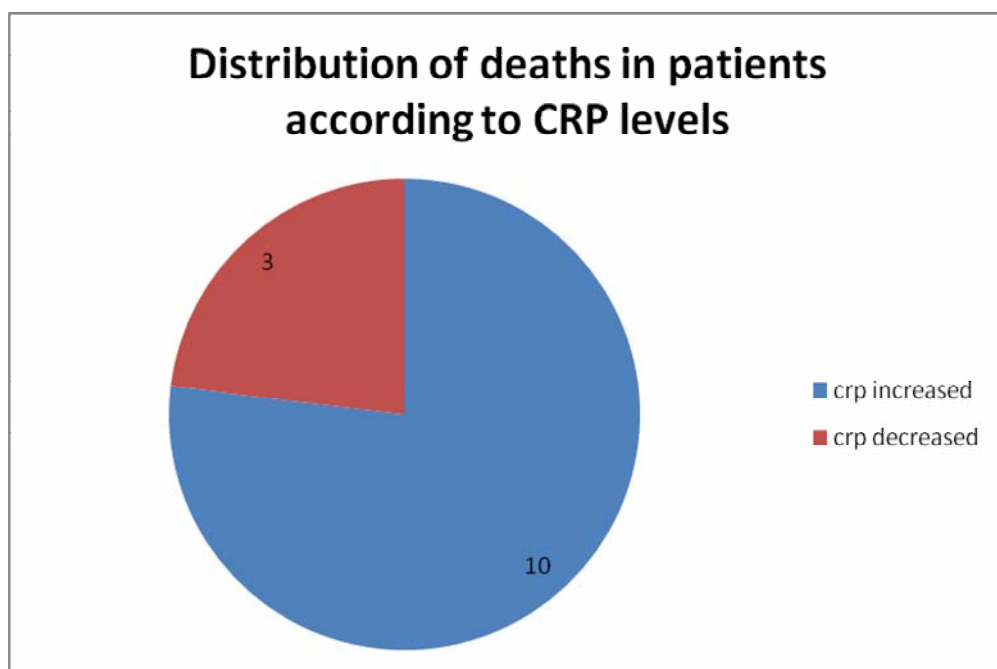
Total number of patients died of CAP were 13(13%). 3(23%) were among the group with decreased CRP levels on day- 4,and 10(77%) were among the group with increased CRP levels on day- 4.

Distribution of patients according to 30 day outcome with unchaged status at discharge:

Table-13

CRP Level	No of Patients
Improved	2
Expired	6

Graph-13
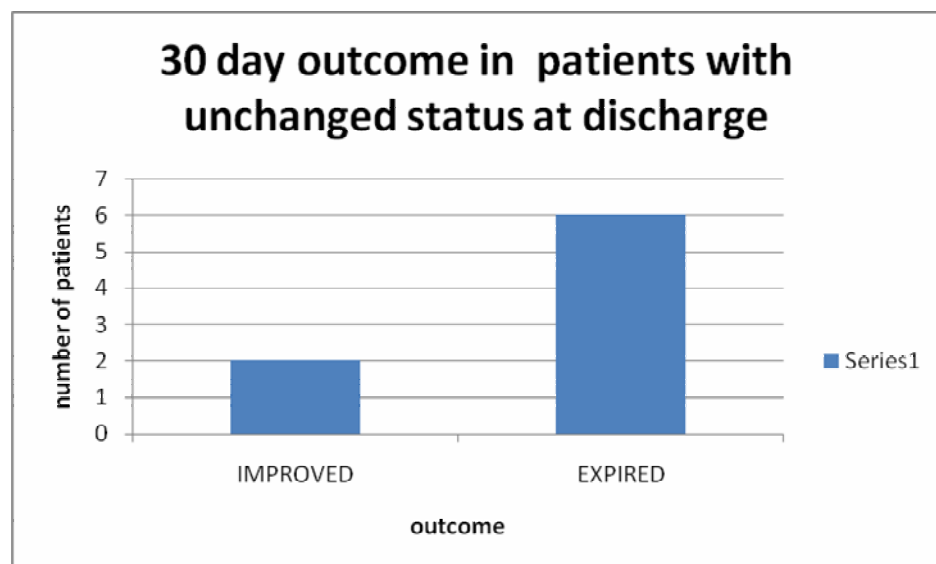
Total number of patients discharged with status as unchanged are 8(8%). Among them 2 (25%) were improved and 6(75%) were expired.

Distribution of deaths in patients with worsened status at discharge according to CRP levels:

Table-14

CRP Level	No of Patients
CRP increased	2
CRP decreased	1

Graph-14
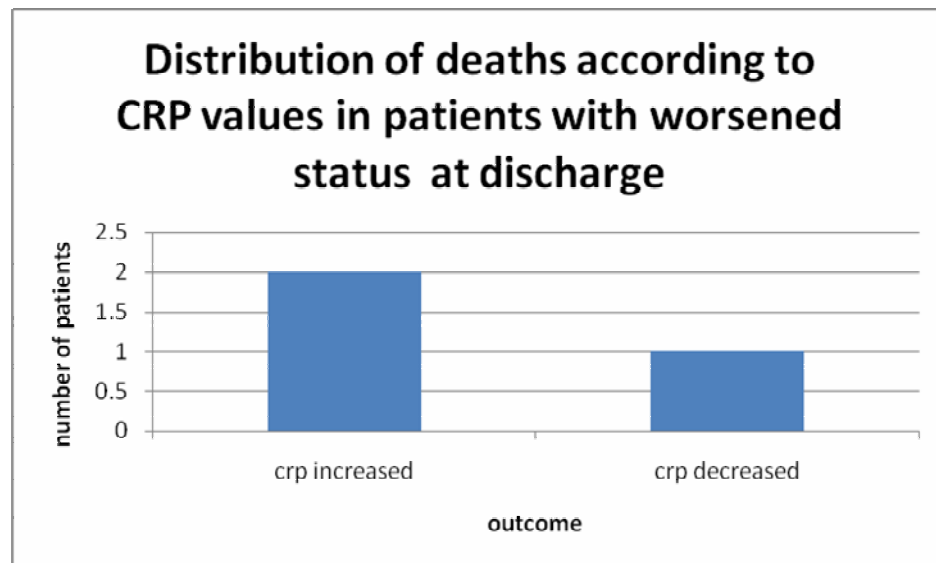
Total number of deaths among the patients with worsened status at discharge were 3(3%). 1(33.3%) was among the group with dereased CRP and 2 (66.6%)were among the group with increased day-4 CRP group.

Distribution of deaths at discharge and at end of 30 days after discharge according to CRP levels:

Table-15

	At discharge	End of 30 days
CRP Increased	2	8
CRP Decreased	2	1

Graph-15
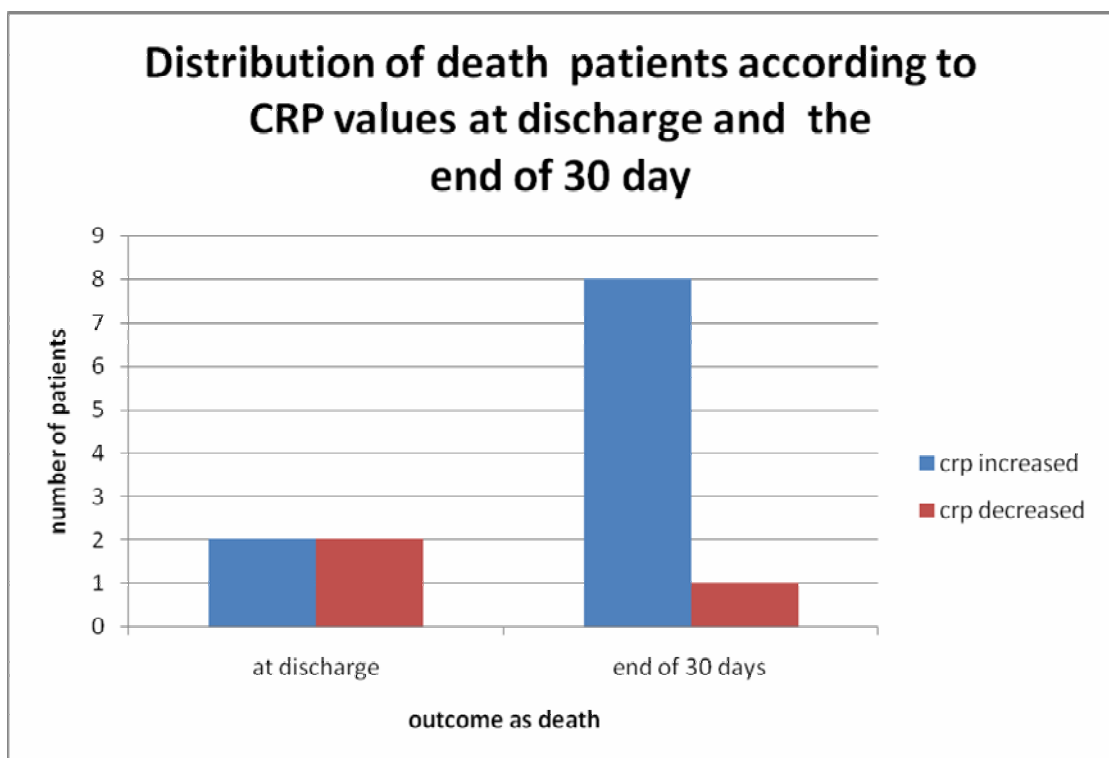
Total number of deaths at discharge were 4(4%) . 2(50%) patients were among the group with increased CRP and 2(50%) were among the group with decreased day-4 CRP.

Total number of deaths by the end of 30 days after discharge were 13(13%) . 3(23%) patients were among the group with decreased crp and 10(77%) were among the group with increased CRP levels on day 4.

Distribution of patients according to need for inotropic support in relation to CRP levels:

Table-16

CRP Level	No of Patients
CRP increased	16
CRP decreased	4

Graph-16
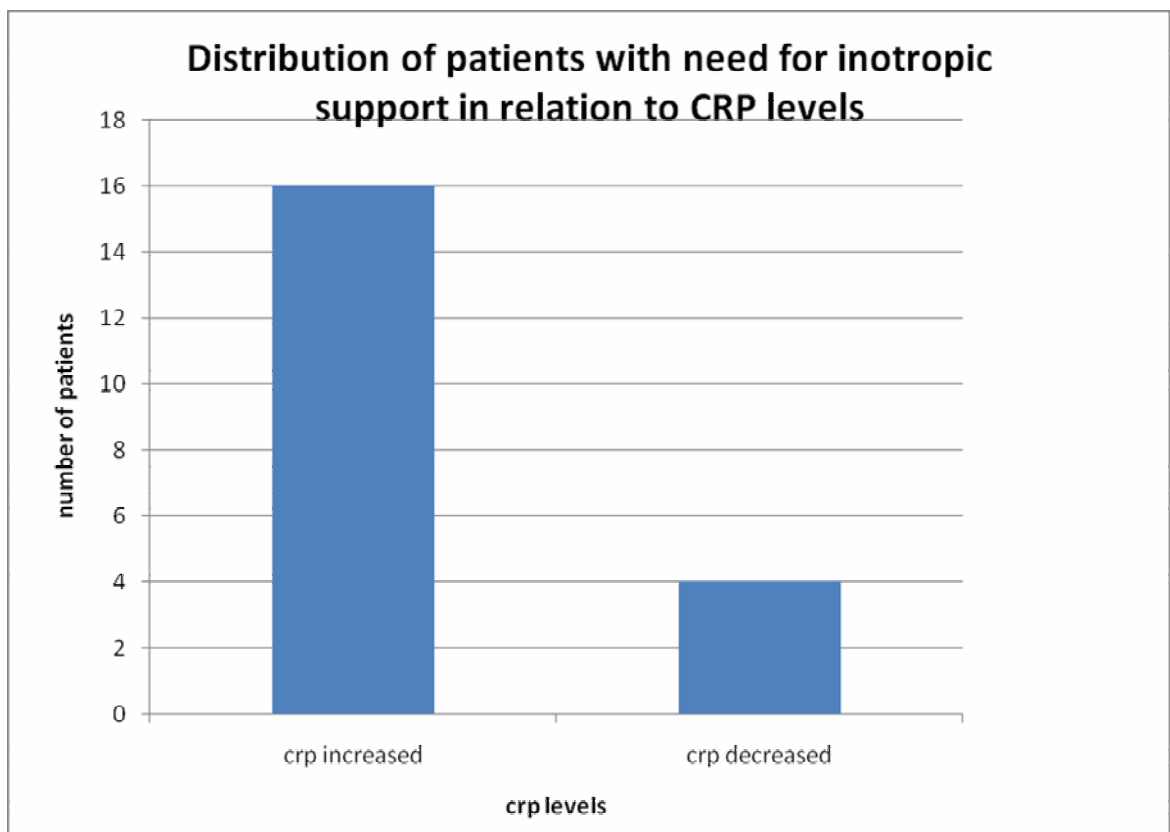
Inotropic support was needed for 20(20%) patients. 16(80%) were among the group with increased day-4 CRP levels, 4(20%) were among the group with day-4 CRP decreased group.

Distribution of patients according to complications developed following CAP:

Table-17

Complication	Patients with CRP increased on day4	Patients CRP decreased on day 4
Respiratory failure	4	1
Shock	3	2
Multiorgan failure	3	1
Lung abscess	2	2
Empyema and need for icd	4	2

Graph -17

Respiratory failure was developed in five(5%) patients.4(80%)were among the group with increased CRP and 1(20%) was among the group with decreased day-4 CRP levels.

Shock was developed in 5(5%)patients.3(60%)were among the group with increased CRP and 2(40%)were among the group with decreased day-4 CRP levels.

Multiorgan failure was developed in 4(4%)patients.3(75%)among the group with increased CRP and 1(25%)was among the group with decreased day-4 CRP levels.

Lung abscess was developed in 4(4%)patients.2(50%)were among the group with increased CRP group and 2(50%)were among the group with day-4 CRP dereased group.

Empyema and need for ICD was needed in 6(6%)patients.4(66.6%)were among the group with CRP increased group and 2(33.3%)were among the group with day-4 CRP decreased group.

STATISTICAL ANALYSIS:

Chi-Square Test:

variables were final outcome at the end of 30 days after discharge and crp levels on day 4 when compared to day-1.

Day 4 CRP levels	Outcome		
	Improved	**Expired**	**Total**
Increased	20	10	30
Decreased	67	3	70
Total	87	13	100

Pearson chi-square value= 15.667

 P value = 0.000.

 In this study P value is 0.000 which is <0.05, so the study is significant. Indicating that raise in CRP level on day-4 when compared to day-1 predicts the outcome in CAP.

Sensitivity is 76%

Specificity is 77%

Positive predictive value is 33.33%

Negative predictive value is 95%

Paired Samples Test :

Variables were levels of CRP on day-1 and day-4

T value= 1.6060

 p value = 0.000

In this study P value is 0.000 which is <0.05, so the study is significant. Indicating that comparision of levels of CRP on day -1 and day-4 prognosticates the outcome in CAP .

DISCUSSION

C –reactive protein is an acute phase protein synthesized by the liver in response to tissue damage. Interleukin -6 is thought to be the primary trigger of CRP release, although tumor necrosis factor-alpha,IL-1,and other cytokines also trigger the release of CRP[1].

Studies have shown that elevated CRP in community acquired pneumonia is independently associated with requirement for inpatient care, that higher CRP levels results in longer duration of hospital stay and poorer clinical outcome. One of the major advantage of CRP is that serial measurements can be taken as a marker of treatment response. In patients admitted to hospital, a CRP level that falls by 50% or more in 4 days indicates a low risk of 30 day mortality, need for ventilation and/or inotropic support, or development of complicated pneumonia[1].

In this study it is observed that community acquired pneumonia is more common in middle aged males. Most common is combined right middle lobe and lower lobe pneumonia.

Commonest organism isolated among culture positive patients is klebsiella pneumonia(14%) followed by staphylococcus areus(12%) then streptococcus pneumonia(5%).However in 65% patients sputum is sterile.

Most of the patients got treated partially in periphery hospitals with different antibiotics were reffered to this tertiary care hospital, hence isolation of causative organism in sputum culture is low. That prior antibiotic use had interfered the sputum culture and sensitivity, even though gram stain had shown gram positive cocci , sputum culture was sterile. All patients were started on higher antibiotics on admission in this

hospital and add on antibiotic was added in few patients according to sputum sensitivity report.

CRP is raised in 30 % patients when compared to the value of CRP on day -1 and day-4, and decreased in 70% patients.

Duration of hospital stay was more in patients with increased day-4 CRP when compared to the patients with decreased day-4 CRP.

At the time of discharge 85% patients were improved, 8% patients status was unchanged, 3% patients status was worsened, and 4% patients were expired.

During the follow up of the patients with status unchanged at discharge, among the 8, six patients were improved and two were expired. All the six patients expired were belong to the group of increased day-4 CRP.

During the follow up of the patients with status worsened at discharge, all three were expired with in twenty four hours of discharge. 2(66%) were among the group with increased day-4 CRP and 1(33.3%) was among the group with decreased day-4 CRP.

Ventilator support was given for five (5%)patients. Among them 4(80%) patients belongs to the group with increased day-4 CRP and 1(20%) patient belong to decreased day-4 CRP.
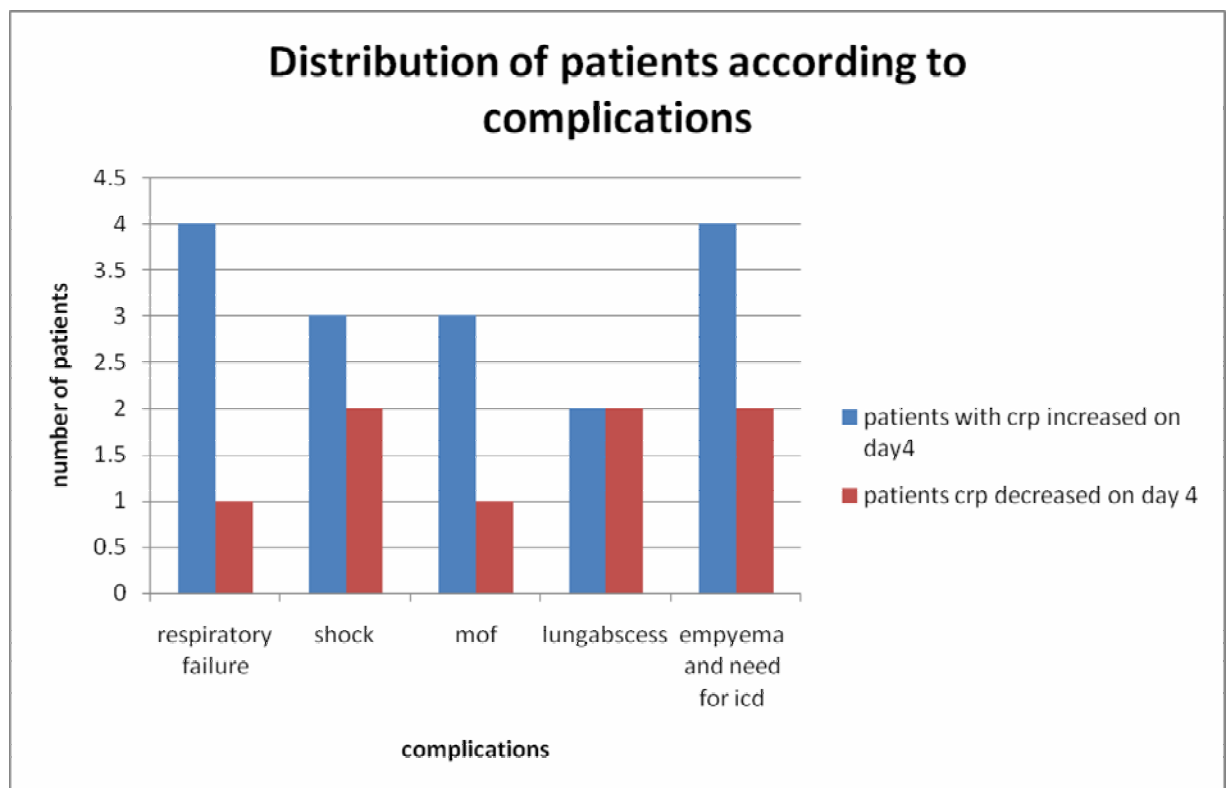
Inotropic support was needed for 20(20%) patients. 16(80%) were among the group with increased day-4 CRP levels, 4(20%) were among the group with decreased day-4 CRP group.

Respiratory failure was developed in five(5%) patients.4(80%)were among the group with increased CRP and 1(20%) was among the group with decreased day-4 CRP levels.

Shock was developed in 5(5%)patients.3(60%)were among the group with increased CRP and 2(40%)were among the group with decreased day-4 CRP levels.

Multiorgan failure was developed in 4(4%)patients.3(75%)among the group with increased CRP and 1(25%)was among the group with decreased day-4 CRP levels.

Lung abscess was developed in 4(4%)patients.2(50%)were among the group with increased CRP group and 2(50%)were among the group with day-4 CRP dereased group.

Empyema and need for ICD was needed in 6(6%)patients.4(66.6%)were among the group with CRP increased group and 2(33.3%)were among the group with day-4 CRP decreased group.

Respiratory failure,Multiorgan failure, and Empyema and need for ICD insertion was high among the group with increased day-4 CRP.

.

Total number of patients died of CAP were 13(13%). 3(23%) were among the group with decreased CRP levels on day- 4,and 10(77%) were among the group with increased CRP levels on day- 4.

Admission level of CRP may not be helpful for predicting course of the patient ,rather than the raising levels does.

This study concludes that if CRP levels raises on day -4 when compared to day -1 ,the length of stay in hospital, need for mechanical ventilator support, need for inotropic support, complications,and mortality increases.

Luis Coelho et al[50] , in their study concluded that daily CRP measurement after antibiotic prescription is useful in identification of severe community acquired pneumonia as early as day 3, in patients with poor outcome. The identification of CRP pattern of response to antibiotic therapy was useful in the recognition of the individual clinical course,either improving or worsening, as well as rate of improvement.

Jordi Almirall et al[51], in their study concluded that , serum CRP level is a useful marker for establishing the diagnosis and prognosis of CAP . High CRP values are suggestive of severity, which may be value in deciding about the appropriateness of inpatient care.

Robin P. Smith Mb et al[52], in their study concluded that, CRP is a sensitive marker of pneumonia. A persistently high or rising CRP level suggests antibiotic failure or the development of an infective complication.

James D. Chalmers et al[53], in their study concluded that, admission CRP<100 mg/l has reduced risk for 30-day mortality, need for mechanical ventilation and /or inotropic support, and complicated pneumonia. Failure of CRP to fall by 50% or more at day 4 leads to increased risk of 30-day mortality, need for mechanical ventilation and/or inotropic support, and complicated pneumonia Ponka and Sarna [54] and Orqvist *et al*. [55] showed that pneumonias caused by *S. pneumoniae*, especially when bacteraemic, were associated with a greater host response (higher levels of IL-6 and CRP) than those caused by other pathogens (*M. pneumoniae* and viruses).

Póvoa, Pedro[65], Serum markers have demonstrated potential value in early prediction and diagnosis of pneumonia, in monitoring the clinical course and in guiding antibiotic therapy. C-

reactive protein appears to perform better in diagnosing infection, because several studies have shown that procalcitonin may remain undetectable in some patients, specifically those with pneumonia.

H. W. Bruns et al[59] , consecutive C-reactive protein measurements are useful in the first week in follow-up of antibiotic treatment for severe community-acquired pneumonia when taking the causative microorganism and use of steroids into account. A delayed normalisation of C-reactive protein levels is associated with a higher risk of having received inappropriate antibiotic treatment.

SUMMARY

This study has been done on 100 consecutive patients presented with Community Acquired Pneumonia admitted to Shri B.M.Patil Medical College Hospital and Research Centre, Bijapur, from October 2008 to May 2010

In this study it was observed that community acquired pneumonia is more common in middle aged males Most common is combined right middle lobe and lower lobe pneumonia.

Commonest organism isolated among culture positive patients was klebsiella pneumonia(14%) followed by staphylococcus areus(12%) then streptococcus pneumonia(5%). How ever 65% patients sputum is sterile.

Most of the patients got treated partially in periphery hospitals with different antibiotics were reffered to this tertiary care hospital.That prior antibiotic use had interfered the sputum culture and sensitivity, and all the patients were started on higher antibiotics on admission in this hospital and add on antibiotic was added in few patients according to sputum sensitivity report.

CRP levels are increased in 30% and decreased in 70% patients, on day-4 when compared to the levels on day -1.

Worsening of CAP occurred in 10(33.3%) patients among the group in which CRP had raised on day-4 and 3(4.28%) patients among the group in which CRP had decreased on day- 4.Mean duration of stay, need for inotropic support, mechanical ventilatory support, complications, and mortality was high among the group with raise in day -4 CRP levels.

Hence this study very well goes in accordance with various other studies done all over the world and summarises that serial estimation of levels of CRP in patients with CAP will predict the prognosis, complications, need for ventilatory support, inotropic support, mortality, and outcome.

CONCLUSION

C-reactive protein is an independent predictor of severity in community acquired pneumonia. This study concludes that if CRP levels raises on day-4 when compared to day-1, the length of stay in hospital, need for mechanical ventilator support, complications, need for inotropic support, and mortality increases.

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B.L.D.E.U'S SHRI B.M.PATIL MEDICAL COLLEGE

HOSPITAL AND RESEARCH CENTRE, BIJAPUR

CRP AS AN INDEPENDENT PREDICTOR OF SEVERITY IN COMMUNITY

ACQUIRED PNEUMONIA

PROFORMA

NAME   :

AGE   :

SEX   :

OCCUPATION   :

RELIGION   :

IP NO   :

ADDRESS   :

DATE OF ADMISSION   :

DATE OF DISCHARGE   :

STATUS AT DISCHARGE :

PRESENTING COMPLAINTS:

Cough with or with out expectoration

Breathlessness

Chest pain

Fever

Associated symptoms

HISTORY OF PRESENTING ILLNESS:

Cough –   Onset

                 Duration

Type

With or with out expectoration

Diurnal variation

Seasonal variation

Sputum –   Duration

Quantity

Postural variation

Colour

Odour

Haemoptysis

Breathlessness – Onset

                 Duration

                 Progress

                 Grade

                 Seasonal variation

                 h/o wheeze

                 h/o orthopnoea

                 h/o paroxysmal nocturnal dyspnoea

Chest pain

        Duration

        Site

        Type

        Radiation

        Aggravating and relieving factors

Fever

        Onset

Type

Duration

Diurnal variation

Associated symptoms

Loss of appetite

Loss of weight

TREATMENT HISTORY

PAST HISTORY:

Hypertension

Diabetes mellitus

Exposure to STD

Tuberculosis

PERSONAL HISTORY:

HABITS:

Smoking

Tobacco chewing

Alcohol consumption

FAMILY HISTORY:

GENERAL PHYSICAL EXAMINATION:

Consciousness

Orientation to Time/ Place/ Person

Pallor

 Icterus

Herpes labialis

Cyanosis

Clubbing

Lymphadenopathy

Pedal odema

VITAL SIGNS:

Pulse

Blood pressure

Temperature

Respiratory Rate

       Rhythm

RESPIRATORY SYSTEM EXAMINATION:

INSPECTION:

Position of trachea

Shape of the chest

Hollowing

Bulging

Flattening

Retraction

SPINAL DEFORMITIES:

Kyphosis

Scoliosis

Respiratory movements:

Rate:

Rhythm

Character

Equality of movements

Accesory muscles of respiration:

Apex beat:

MISCELLANEOUS:

Scars, sinuses:

Visible pulsations:

Dilated veins:

PALPATION:

Position of trachea:

Measurement of chest expansion:

Apex beat :

Tactile vocal fermitus:

PERCUSSION:

AUSCULTATION:

Type of breath sounds:

Added sounds:

EXAMINATION OF OTHER SYSTEMS :

CARDIOVASULAR SYSTEM:

PER ABDOMEN:

CENTRAL NERVOUS SYSTEM:

PROVISIONAL DIAGNOSIS:

INVESTIGATIONS

I.HAEMATOLOGY

HB%	Gm/dl
TC	Cells/mm ^{3}
DC	
NEUTROPHILS	%
LYMPHOCYTES	%
EOSINOPHILS	%
BASOPHILS	%
MONOCYTES	%
ESR	%
PERIPHERAL SMEAR STUDY	

II. URINE EXAMINATION

Sugar	
Albumin	
Microscopy	

III. BIOCHEMISTRY

RANDOM BLOOD SUGAR	
BLOOD UREA	
SERUM CREATININE	
CRP LEVELS ON DAY OF ADMISSION	
CRP LEVELS ON 4TH DAY OF ADMISSION	

IV.CHEST X- RAY

PA VIEW

LATERAL VIEW

V. SPUTUM EXAMINATION:

SPUTUM AFB

GRAM STAIN

CULTURE AND SENSITIVITY

MALIGNANT CELLS

VI. CT SCAN CHEST

VII. ECG

VIII. FIBER OPTIC BRONCHOSCOPY

IX FINAL DIAGNOSIS

X. TREATMENT

XI. FOLLOW UP

SHRI B.M. PATIL MEDICAL COLLEGE, HOSPITAL AND

RESEARCH

CENTRE, BIJAPUR – 586103.

CONSENT FORM

TITLE OF RESEARCH   : "C-REACTIVE PROTEIN AS AN INDEPENDENT PREDICTOR OF SEVERITY IN COMMUNITY ACQUIRED PNEUMONIA"

GUIDE   :   DR. M. S. BIRADAR

P.G. STUDENT   :   DR. CHANDRAKANTH TAPSI

PURPOSE OF RESEARCH:

I have been informed that the purpose of this study is to evaluate the significance of C-reactive protein as predictor of severity in community acquired pneumonia

PROCEDURE :

I understand that I will undergo detailed history and clinical examination and investigations.

RISKS AND DISCOMFORTS: I understand that there is no risk involved and I may experience mild pain during the above-mentioned procedures.

BENEFITS:

      I understand that my participation in this study will help in evaluation of CRP levels as an independent predictor of severity in community acquired pneumonia.

CONFIDENTIALITY:

      I understand that the medical information produced by the study will become a part of hospital record and will be subjected to confidentiality and privacy regulations of hospital. If the data is used for publications the identity of the patient will not be revealed.

REQUEST FOR MORE INFORMATION:

      I understand that I may ask for more information about the study at any time.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:I understand that my participation is voluntary and I may refuse to participate or withdraw for study at any time.

INJURY STATEMENT:

      I understand in the unlikely event of injury to me during the study I will get medical treatment but no further compensations.

(Signature of Guardian)   (Signature of patient)

(If the patient is conscious, well oriented and fully aware)

KEY TO MASTER CHART:

SEX:　　　**1=Male**

　　　　　　2=Female

Culture :　　**0=sterile**

　　　　　　1=Pneumoccocus pneumoniae

　　　　　　2=Staphyloccocus areus

　　　　　　3=E.Coli

　　　　　　4=Klebsiella pneumonia

Diagnosis :　**1=right upper lobe pneumonia**

　　　　　　2=right middle lobe pneumonia

　　　　　　3=right lower lobe pneumonia

　　　　　　4=right upper and middle lobe pneumonia

　　　　　　5=right middle and lower lobe pneumonia

　　　　　　6=right sided extensive pneumonia

　　　　　　7=left upper lobe pneumonia

　　　　　　8=left lower lobe pneumonia

　　　　　　9=left sided extensive pneumonia

　　　　　　10=bilateral extensive pneumonia

Antibiotics:　**1=levofloxacin**

　　　　　　2=ceftriaxone+sulbactum

　　　　　　3=pipericillin+tazobactum

　　　　　　4= pipericillin+tazobactum+levofloxacin

　　　　　　5=pipericillin+tazobactum+amikacin

6=pipericillin+tazobactum+levofloxacin+ornidazole

7= ceftriaxone+sulbactum+levofloxacin

Outcome: **1=improved**

        2=unchanged

        3=worsened

        4=expired

CRP Levels: **1=increased**

        2=decreased

        3=same

MASTER CHART

Sl.no	Name	Age	Sex	Ip.number	CRP-day1	CRP-day4	CRP inf	Culture	Diagnosis	Duration of stay	Interval	Outcome at discharge	Final outcome	Antibiotic used
1	IMAMSAB	60	1	1500	3.2	1.2	2	0	2	12	2	1	1	2
2	BASAPPA	30	1	13623	6	4	2	4	10	12	2	1	1	3
3	RAMAGOND	22	1	15272	10	11	1	2	10	15	2	1	1	3
4	SAIMUDDIN	50	1	1492	4.2	5	1	0	3	20	3	2	4	3
5	SHARANAPPA	29	1	2456	3.2	4	1	0	5	14	2	1	1	4
6	DODAWWA	50	2	1076	5.1	6	1	0	1	10	1	1	1	4
7	YAKUB	55	1	9832	6	2	2	1	7	10	1	1	1	4
8	MERAMMA	45	2	7360	6	2	2	0	3	13	2	1	1	4
9	DUNDAWWA	50	2	2781	4	2	2	0	5	14	2	1	1	4
10	KASTURI	30	2	16346	6	2	2	0	5	13	2	1	1	4
11	CHENNAPPA	34	1	3378	8	4.3	2	0	2	10	1	1	1	4
12	IRAGANTI	22	1	4528	10	6	2	4	10	10	1	1	1	4
13	BASALINGAYA	34	1	1130	4.9	2.4	2	0	5	12	2	1	1	4
14	MALLEASAPPA	45	1	10586	7.8	3	2	0	3	9	1	1	1	4
15	HARI	23	1	4561	5	6	1	0	3	8	1	1	1	4
16	SHIVAPPA	45	1	1432	4	3.4	2	0	5	12	2	1	1	4
17	PARASAPPA	34	1	6934	7	4.3	2	4	6	15	2	1	1	4
18	SUBASH	23	1	5481	5.6	3.7	2	0	5	13	2	1	1	4
19	NARAYANA	23	1	3490	6.7	3.5	2	0	3	10	1	1	1	4
20	ASHOK	34	1	7041	4.1	2.3	2	0	3	12	2	1	1	4

21	KRISHANAPPA	56	1	10974	6.5	3	2	0	5	11	2	1	1	4
22	MURTUSAB	34	1	2337	3.6	5	1	0	5	9	1	1	1	4
23	TULJAPPA	45	1	4829	4.6	4	2	2	10	17	3	1	1	4
24	BHIMASHANKAR	58	1	13409	7.8	5.6	2	3	5	20	3	1	1	4
25	NEELAPPA	34	1	4092	4.3	2.3	2	0	3	12	2	1	1	4
26	BHIMARAYA	23	1	209	3.4	1.9	2	0	3	7	1	1	1	4
27	LAKSHMAN	47	1	2046	4.9	5	1	4	5	10	1	1	1	4
28	SIDDAPPA	54	1	5129	5.1	7	1	0	2	9	1	1	1	4
29	MAHADEVAPPA	41	1	10389	4.6	3	2	0	2	8	1	1	1	4
30	MANNU CHAVAN	46	1	12478	5.6	2.9	2	0	3	10	1	1	1	4
31	BASAVARAJ	25	1	904	6.7	3.6	2	0	5	9	1	1	1	4
32	GODABAI	51	2	14289	4	4	2	0	5	12	2	1	1	4
33	SAHEBGOUDA	42	1	11383	3.8	2	2	0	2	10	1	1	1	4
34	VASANTHA	31	2	1231	5.6	1.8	2	0	2	8	1	1	1	4
35	KUMAR	24	1	11510	4.5	3.9	2	0	3	7	1	1	1	4
36	RAJASAB	56	1	2360	5.6	4	2	0	2	10	1	1	1	4
37	LALITHABAI	38	2	15750	4.8	3.1	2	1	3	10	1	1	1	4
38	MUTTAPPA	34	1	12078	4	2	2	0	5	10	1	1	1	4
39	KENCHAWWA	26	2	2384	5	3.5	2	4	10	10	1	1	1	4
40	HIREMATH	48	1	11890	4.1	3.2	2	0	3	12	2	1	1	4
41	ABDUL	34	1	10894	7	5	2	4	6	15	2	1	1	4
42	SATTEWWA	41	2	12580	5.4	3.9	2	0	5	14	2	1	1	4
43	KARIMSAB	32	1	3694	6	3.7	2	0	5	12	2	1	1	4
44	PREM SINGH	24	1	1280	7.2	3.2	2	0	2	8	1	1	1	4
45	HANUMANTH	31	1	2583	4	2	2	0	2	10	1	1	1	4
46	ANNAPPA	50	1	106	22	24	1	0	3	14	2	2	4	4
47	JANABAI	56	2	26	0.5	2.4	1	0	5	10	1	2	1	4

48	NINGAPPA	48	1	2845	4.3	5.3	1	2	5	20	3	3	4	4
49	DONGRISAB	39	1	4801	7.8	9.7	1	2	10	6	1	4	4	4
50	MALLAPPA	40	1	15721	9	3	2	4	3	14	2	1	1	5
51	MEENAXI	22	2	2389	14	6	2	0	8	12	2	1	1	6
52	SHANTAPPA	45	1	8543	8	3.6	2	3	10	16	3	2	1	6
53	MUDAKAPPA	32	1	2379	9	9	2	3	10	15	2	2	4	6
54	KAREPPAGOUDA	35	1	1656	2.2	3.2	1	2	2	20	3	3	4	6
55	GODABAI	45	2	11490	1.6	5.6	1	2	5	20	3	3	4	6
56	SAKUBAI	42	2	1312	10	12	1	0	5	12	2	4	4	6
57	RAMESH	17	1	12075	6	8	1	4	10	16	3	4	4	6
58	SUSLABAI	46	2	14782	10	11	1	4	10	6	1	4	4	6
59	MANJUNATH	18	1	1736	5.2	1.2	2	0	10	14	2	1	1	7
60	SHIVABASAPPA	45	1	690	8	1.2	2	0	7	15	2	1	1	7
61	BASAPPA	48	1	1469	2.2	0.9	2	0	4	10	1	1	1	7
62	SHANKURABAI	58	2	2963	4.6	6	1	0	10	14	2	1	1	7
63	GAURAWWA	44	2	11568	5.1	4.8	2	0	7	10	1	1	1	7
64	NEELAMMA	48	2	12890	4.6	4.2	2	2	7	14	2	1	1	7
65	KARANU	51	1	1544	5.4	1.6	2	0	2	13	2	1	1	7
66	GOVIND	28	1	1846	6	7	1	2	5	14	2	1	1	7
67	SIDDALINGAYYA	43	1	1355	4.6	3.1	2	0	5	10	1	1	1	7
68	BHIMARAYA	40	1	7932	5.8	2.2	2	2	3	12	2	1	1	7
69	MALLAYA	42	1	8340	6	2	2	0	9	17	3	1	1	7
70	BASALINGAYA	34	1	4658	4	4.6	1	0	1	10	1	1	1	7
71	KAVITHA	21	2	8338	3.3	1.6	2	0	7	10	1	1	1	7
72	MAHADEV	39	1	5185	3.9	4	1	0	10	10	1	1	1	7
73	RANGU CHAVAN	46	1	1988	4.6	2.1	2	2	6	14	2	1	1	7
74	IBHRAHIMSAB	56	1	3068	4.9	6	1	2	10	10	1	1	1	7

75	BHIMANNA	34	1	2459	6.2	3.2	2	1	6	13	2	1	1	7
76	BASAPPA	20	1	4356	5.4	1.6	2	0	10	14	2	1	1	7
77	BASAYYA	35	1	8575	9	4	2	4	10	15	2	1	1	7
78	HUSSAIN	30	1	1278	4	1	2	1	3	12	2	1	1	7
79	RAZAKBI	34	2	5095	7	3	2	2	6	10	1	1	1	7
80	ADEPPA	37	1	6954	8	2	2	3	3	14	2	1	1	7
81	HANAMANTH	35	1	11376	8	3	2	4	10	12	2	1	1	7
82	RENUKA	42	2	3276	7	8	1	4	10	14	2	1	1	7
83	DHAREPPA	32	1	2285	4	2	2	0	2	8	1	1	1	7
84	SADHASHIV	23	1	1054	5	2.3	2	0	2	8	1	1	1	7
85	NINGAPPA	57	1	11043	6	1.4	2	0	3	7	1	1	1	7
86	KALLAPPA	41	1	2249	8.7	2.4	2	2	5	10	1	1	1	7
87	MURAGAAPA	28	1	12589	5	6	1	0	3	10	1	1	1	7
88	GURUPADAPPA	57	1	16734	8	9	1	0	5	14	2	1	1	7
89	SANGAMMA	34	2	13632	9	3	2	2	5	13	2	1	1	7
90	CHANDRAM PUJERI	45	1	14571	5.8	6	1	0	3	10	1	1	1	7
91	BASAPPA	29	1	3420	5	7	1	0	5	10	1	1	1	7
92	NAGARAJ	23	1	4590	6	2	2	0	5	10	1	1	1	7
93	LAKSHMIBAI	54	2	4780	4.5	3	2	0	5	10	1	1	1	7
94	VANAYAK	43	1	6709	5.4	6	1	0	3	14	2	1	1	7
95	BASAYYA HIREMATH	51	1	12509	4	3	2	0	7	10	1	1	1	7
96	KAJASAB	29	1	2074	6	2	2	1	3	12	2	1	1	96
97	BABUGOUDA	28	1	3491	6	7	1	0	5	14	2	1	1	7
98	RAFIQ	19	1	1537	5.2	6	1	0	2	10	1	2	4	7
99	GURAPPA	45	1	9671	5.6	4.8	2	0	10	10	1	2	4	7
100	SHEKAPPA	40	1	3409	5	5	2	0	3	10	1	2	4	7