Role of CRP in Lower Respiratory Tract Infections

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Abstract

Introduction: Better diagnostic tests that establish the cause of LRTIs can reduce irrational antibiotic use. CRP is an acute phase protein that increases on inflammatory triggers can solve the purpose. The study aimed at role of CRP in distinguishing between bacterial and viral etiology. **Materials and Methods**: Fifty patients, aged 2 months to 5 years, with complaints of fever, cough and respiratory distress were included. Along with all other basic investigations like CBC, PBF, ESR, CRP Quantitative was also by Nycocard CRP Single Test for in vitro rapid determination. **Results**: In LRTI of probable bacterial aetiology mean CRP was 61.72 ±36.665 mg/l which was significantly higher than those with probable viral aetiology with mean CRP of 5.24 ±1.4 mg/l. The cut off level of CRP is taken as 9 mg/l with sensitivity of 100% and specificity of 96 %. **Conclusion**: CRP levels are both sensitive and specific for differentiating between viral and bacterial LRTI, thus reducing the overuse of antibiotics in clinical practice.

Key words: Lower respiratory tract infections, C-reactive protein.

Introduction

C-reactive protein (CRP) is an acute phase protein that increases on inflammatory triggers and decreases rapidly with resolution of inflammation. It is synthesized and secreted by the liver in response to inflammatory cytokines, particularly IL-6 and others such as tumour necrosis factor (TNF), IL-I and transforming growth factor[1,2]. CRP synthesis increases within 4-6 hours of an inflammatory trigger and doubles every 8 hours. It peaks at 36 to 50 hours[3]. The ability to measure CRP quickly and quantitatively has made it increasingly useful in clinical practice. The definition of the presence, the aetiology and the severity of lower respiratory tract infection (LRTI) as well as the treatment choice and duration are frequently a real problem for the treating physician. Clinical features are sometimes misleading and not specific varying according to the aetiology (bacterial or viral), virulence, and adequacy of host response and presence of concomitant diseases. The aetiology is also poorly established due to inadequate patient definition and limited pathogen detection (16–55%) resulting from a combination of inadequate clinical sampling and pathogen detection methodology, particularly for respiratory viruses[4,5]. Excessive use of antibiotics is the main cause of the spread of antibiotic-resistant bacteria[6,7]. Thus, avoidance of irrational antibiotics is essential to combat emergence of antibiotic-resistant micro-organisms[8,9]. In view of this diagnostic and therapeutic dilemma, a more reliable test for the differential diagnosis of bacterial respiratory tract infections in need of antibiotics from other respiratory disease would be extremely helpful[10]. There is a clear need for diagnostic and prognostic biomarkers in LRTIs. The aim of this study was to find out about the role of CRP in distinguishing between bacterial and viral etiology of LRTI

Materials and Methods

This was a prospective study. The subjects included 50 patients in the age group of two months to five years of either sex with complaints of fever, cough and fast breathing attending the indoor and OPD of the department of Paediatrics of Sri Guru Ramdas Institute of Medical Sciences and Research, Amritsar. Diagnosis of lower respiratory tract infections was made according to WHO criteria.

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Exclusion criteria

a) Immuno-compromised patients.
b) Patients with congenital heart disease.
c) Patients with congestive heart failure.
d) HIV positive patients

A detailed history and complete clinical examination was done. The subjects were screened for Hb, TLC, DLC, PBF, ESR and Quantitative CRP. Chest X-ray (PA view) was done in all cases and USG or CT chest was done whenever indicated.

CRP was done by Nycocard CRP single test, an in vitro test that is used for the rapid determination of CRP. Nycocard CRP single test is a solid phase, sandwich format, immunometric assay. In this test there is a membrane coated with immobilised CRP-specific monoclonal antibodies. A diluted sample is applied to the test device. When the sample flows through the membrane, the C reactive proteins are captured by the antibodies. CRP trapped on the membrane will then bind the gold–antibody conjugated added, in a sandwich type reaction. A paper layer underneath the membrane absorbs excess liquid. In the presence of pathological level of CRP in the sample, the membrane appears red-brown with colour intensity proportional to the CRP concentration of the sample. The colour intensity is measured quantitatively with the NYCO card Reader. The data was analysed by chi-square test using SPSS 15.0 version software

Results

CRP was found to be 61.72 ± 36.665 mg/l in patients with bacterial aetiology. And those with probable viral aetiology (e.g. bronchiolitis) had mean CRP of 5.24 ±1.411 mg/l. The mean difference was found to be 56.486 and *p*-value is less than 0.001 that is highly significant.

The receiver-operating characteristic curve area under the curve for relative CRP variation was 0.973 (95% confidence interval = 0.61–0.86). The larger the area, the better is the diagnostic test.

Table 2: Depicting the cut off value of CRP

Positive if less than or equal toa	Sensitivity	1 – Specificity
2.00	.000	.000
3.50	.048	.000
4.50	.381	.034
5.50	.619	.034
6.50	.810	.034
7.50	.905	.034
9.00	1.000	.034
11.00	1.000	.103
18.00	1.000	.172
28.00	1.000	.207
35.00	1.000	.241
39.00	1.000	.276
42.50	1.000	.310
45.50	1.000	.345
47.00	1.000	.379
50.50	1.000	.414
53.50	1.000	.448
55.50	1.000	.483
61.00	1.000	.517
68.50	1.000	.552
73.00	1.000	.586
74.50	1.000	.655
76.50	1.000	.690
81.50	1.000	.724
87.50	1.000	.759
95.00	1.000	.793
106.00	1.000	.828
116.00	1.000	.862
121.00	1.000	1.000

The cut-off CRP level for differentiating bacterial and viral aetiology on 7.5 mg/l the sensitivity is 90.5% with the specificity of 96%. But if we take 11 mg/l as a cut-off the sensitivity is100% but specificity decreases to 89.7%. So we take 9 mg/l as cut of level of CRP with sensitivity of 100% and specificity of 96 %.

Table 1: Showing the correlation of CRP with bacterial and viral LRTI

Group	N=50	Mean ± SD (mg/l)	Mean difference	't' value	p-value
Bacterial	29	61.72±36.665	56.486	7.038	<0.001*
Viral	21	5.24±1.411			

*$p < 0.001$; Highly significant

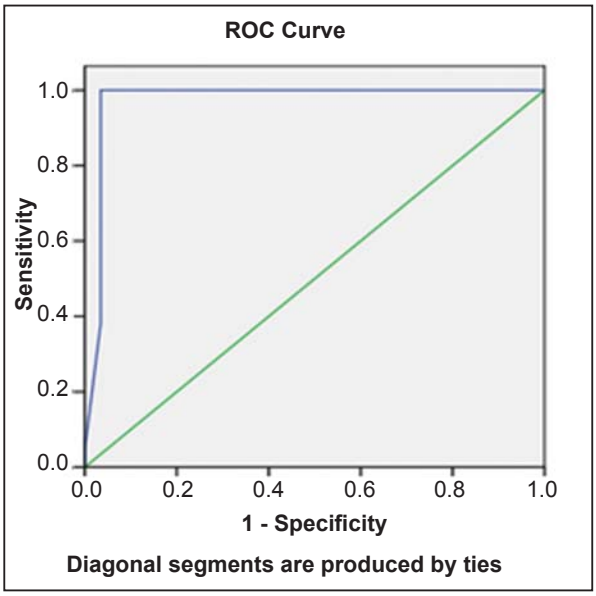

Fig 1: ROC Curve showing sensitivity and specificity of CRP.

Discussion

Irrational prescription of antibiotics for respiratory tract infections is partly caused by diagnostic uncertainty about aetiology. Tests for C reactive protein are increasingly used to guide antibiotic prescribing for infections of the lower respiratory tract.

In this study, in LRTI of bacterial aetiology mean CRP was found to be 61.72 ± 36.665 mg/l and those with probable viral aetiology had mean CRP of 5.24 ±1.411. Similar observations were made by Smith et al[11] who observed mean CRP in pneumonia is 217 ± 16 mg/l and in bronchiolitis mean CRP is 18 ± 3 mg/l. Though the levels of CRP in our study are lesser than in the study by Smith et al, it could be because of prior antibiotic use, single measurement of CRP in our study, varied time interval of presentation and inclusion only of uncomplicated cases of pneumonia. Flanders et al[12] also evaluated median CRP levels which were significantly higher for patients with pneumonia than viral LRTI (60 mg/l versus 9 mg/l; P < 0.001). Dagga et al[13] observed that the mean CRP was 75.87±17.1 mg/l in patients with pneumonia and 16.71±20.76mg/l in patients with COPD in acute exacerbation. Mean CRP levels were 121.3+/-122 and 27.2+/-26 mg/l, respectively in bacterial and viral LRTI in study conducted by Marcus et al[14] .The study aimed at differentiating bacterial and viral LRTI and CRP levels were higher in former than later.

In present study the receiver-operating characteristic curve area under the curve for relative CRP variation was 0.973 (95% confidence interval = 0.61–0.86). Lala SG et al[15] also assessed the discriminative ability of CRP values by ROC plots in pneumonia and found it to be 0.80.This was similar to observation made by Flanders et al[12] who got 0.83 area.

The cut-off of 9 is taken as the best chosen CRP value in this study with 100% sensitivity and specificity of 96.6%. In a similar study by Pullium et al[16] a CRP cut-off point of 7 was determined with sensitivity of 79% and specificity of 91%. Lala SG et al[15] concluded that CRP ≥10 mg/l identified 90% of all bacteraemic pneumonias. The optimal cut off point for CRP 4.4 mg/l achieved a sensitivity of 63% and specificity of 81% for detection of occult bacterial infection in Daniel J et al study[17]. The difference in the cut off values can be explained by different techniques of CRP measurements used in different studies. Inspite of difference in cut-off values, the sensitivity and specificity is significant to help differentiate bacterial and viral LRTI.

Conclusion

CRP is a reliable biomarker to differentiate bacterial and viral LRTI, thus it can empower physicians to safely prescribe lesser and appropriate antibiotics reducing the over usage, toxicity and resistance of antibiotics.

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