



A prospective study of congestive cardiac failure and its prognostication with 3C: Reactive protein as a marker of severity

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Abstract

Background: C reactive protein (CRP), as a marker of inflammation, has been shown to be associated with an increased risk of various cardiovascular diseases. This study is mainly designed to evaluate the level of CRP in patients with chronic CHF and to examine the relation between the degree of CRP elevation and clinical outcome.

Objectives

1. Clinical & Echocardiographic evaluation of patients with congestive cardiac failure.
2. To estimate CRP levels in these subjects.
3. To correlate the CRP levels with severity of the disease.

Material and Methods: A cross sectional study was undertaken among the patients between 18-80 years with congestive cardiac failure who were admitted at ESIC MEDICAL COLLEGE & PGIMSR. A total of 100 cases admitted constituted the sample size. The data for this study was collected by evaluating the patient in the form of detailed history taking, clinical examination, and relevant investigations for this study. Baseline clinical evaluation, 2D echo screening, C-reactive protein estimation was conducted for all the patients. Patients with CCF were divided into two groups: mild CHF (NYHA class 1&2) and severe (CHF NYHA class 3 & 4) groups.

Results: About 52% of the study subjects had Mild (NYHA class 1 & 2) of cardiac failure. Most of the study subjects in this study belonged to 51 – 60 years X of age group. About 53.8% of the patients with mild disease (NYHA class 1 & 2) were males and 64.6% of the patients with severe disease (NYHA class 3 & 4) were females as shown by this study. About 69.2% of the patients with mild disease (NYHA class 1 & 2) and 77.1% with the severe disease (NYHA class 3 & 4) had history of hypertension. Palpitation was present in 21.2% of the patients with mild disease (NYHA class 1 & 2) and 18.8% of the severe disease (NYHA class 3 & 4). Difficulty in breathing was present in 21.2% of the patients with mild disease and 16.7% of the patients with severe disease (NYHA class 3 & 4). S had positive and significant correlation and isovolumetric relaxation time had negative and significant correlation time in mild disease patients. In patients with severe disease, S and E/E was had negative and statistically significant correlation. XI

Conclusion: This study had shown that most of the heart failure patients were aged above 50 years, males, with patients having comorbidities. The CRP had correlation with some echocardiographic parameters. This study had shown that CRP is an important prognostic marker in chronic heart failure.

Keywords: c - reactive protein, congestive cardiac health failure, echo cardiograph, nyha classification, inflammation

Introduction

In mild disease group (NYHA class The patients with mild disease (NYHA class 1 & 2), the correlation coefficient of E was 0.14, A was -0.087, S was 0.349, E/E was 0.21, E/A was -0.025, Deceleration was 0.236, isovolumetric relaxation time (ms) was 0.312, septal wall thickness was -0.185, left ventricular mass index (g/m²) was -0.063, left atrial volume index was -0.076, left ventricular end diastolic volume was 0.113, left ventricular end systolic volume was - 0.282 and ejection fraction was 0.032. In patients with severe disease, the correlation coefficient of E was 0.093, A was -0.081, S was -0.531, E/E was 0.316, E/A was -0.014, Deceleration was -0.043, isovolumetric relaxation time (ms) was -0.192, septal wall thickness was -0.044, left ventricular mass index (g/m²) was -0.063, left atrial volume index was 0.183, left ventricular end diastolic volume was -0.205, left ventricular end systolic volume was -0.137 and ejection fraction was -0.502. The mean (± SD) C reactive protein levels in patients

with mild disease (NYHA 1 & 2) was 4.86 mg/L and mg/L in the patients with severe disease (NYHA class 3 & 4).

Congestive Cardiac Failure (CCF) is a worldwide phenomenon that affects millions of people yearly and carries a high mortality. It is complex syndrome, which is characterized by shortness of breath, fatigue, congestion and cachexia and symptoms related to inadequate tissue perfusion, fluid retention and neurohormonal activation. Despite significant improvement in medical therapy of cardiovascular diseases, CHF remains a serious clinical problem. It represents a major public health burden with high morbidity and mortality. Virtually any cardiac disease may land up in cardiac failure, though the initial event leading to the development of this syndrome in many cases remains unknown.1 Despite repeated attempts to develop a mechanistic definition that encompasses the heterogeneity and complexity of heart failure (HF), no single conceptual paradigm has withstood the test of time. The current American College of Cardiology

Foundation (ACCF)/American Heart Association (AHA) guidelines define HF as a complex clinical syndrome that results from structural or functional impairment of ventricular filling or ejection of blood, which in turn leads to the cardinal clinical symptoms of dyspnoea and fatigue and signs of HF, namely edema and rales. Currently 5.7 million people in the US have HF, but the projections are worrisome since it is expected that by 2030 more than 8 million people will have this condition, accounting for 46% increase in prevalence.²

HF is a burgeoning problem worldwide, with more than 20 million people affected. The overall prevalence of HF in the adult population in developed countries is 2%. HF prevalence follows an exponential pattern, rising with age, and affects 6- 10% of people over age 65.³

The causes of HF and demographic of the patients suffering are not uniformly distributed and great geographic variance exists. Observational studies shows that, hypertension, rheumatic heart disease (RHD) and idiopathic cardiomyopathies are the main causes of heart failure in a significantly younger group of patients when compared to those of developed countries.^{4, 5}

There is no definitive diagnostic test for heart failure, it remains a clinical diagnosis that is largely based on a careful history and physical examination and supported by ancillary test such as chest radiograph, electrocardiogram and echocardiography.⁶

There are 2 mechanisms of reduced cardiac output and heart failure: systolic dysfunction and diastolic dysfunction. The most common causes of systolic dysfunction are ischemic heart disease, idiopathic dilated cardiomyopathy, hypertension and valvular heart disease. Diastolic dysfunction may occur in up to 40 – 50% of the patients with heart failure, it is more prevalent in women, and it increases in frequency with each decade of life. Diastolic dysfunction can occur in many of the same conditions that lead to systolic dysfunction. The most common causes are hypertension, ischemic heart disease, hypertrophic cardiomyopathy and restrictive cardiomyopathy. Many patients who have symptoms suggestive of heart failure including shortness of breath, peripheral edema, paroxysmal nocturnal dyspnoea but also have preserved left ventricular function may not have diastolic dysfunction: instead, their symptoms are caused by other aetiologies, such as lung disease, obesity or occult coronary ischemia.⁷

The research available shows that the CHF should be seen as neurohormonal mode, in which the syndrome of CHF progress because of activation of neurohormones and proinflammatory cytokines following an initial cardiac insult or injury or a mutation of genetic programme, over expression of these biologically active molecules exerts toxic effects on the heart and circulation.^{8, 9}

Activation of the immune system has been implicated in the pathogenesis of CHF. Experimental studies have shown that the known biologic effects of proinflammatory cytokines could explain many aspects of syndrome of heart failure, such as LV dysfunction, pulmonary oedema & process of left ventricular remodelling. The inflammatory marker that presently seems most suitable to assess inflammation is CRP.¹⁰ Cytokines such as tumour necrosis factor alpha (TNF – α) and interleukin – 6 are significantly elevated, producing negative inotropic effects on the heart and the levels of these cytokines may be negatively associated with prognosis.¹¹

C reactive protein (CRP), as a marker of inflammation, has been shown to be associated with an increased risk of various cardiovascular diseases.¹² The serum concentration of CRP is also elevated in patients with congestive heart failure (CHF).¹³ A study reported that increased CRP was an independent predictor of incident CHF in a community based elderly population.¹⁴

The likely reason for this is that the mildly elevated CRP concentrations in these patients fall well within the range found in healthy subjects, and the standard clinical assays for CRP lack sensitivity within the low-normal range: thus they cannot be used effectively for cardiovascular risk prediction. Since high-sensitivity commercial assays for CRP are now available and it can be hypothesized that measurement of CRP might provide prognostic information in these patients.¹⁵

This study is mainly designed to evaluate the level of CRP in patients with chronic CHF and to examine the relation between the degree of CRP elevation and clinical outcome.

Aim and Objectives

Objectives

1. Clinical & Echocardiographic evaluation of patients with congestive cardiac failure.
2. To estimate CRP levels in these subjects.
3. To correlate the CRP levels with severity of the disease.

Material and Methods

A cross sectional study was undertaken among the patients between 18-80 years with congestive cardiac failure who were admitted at ESIC MEDICAL COLLEGE & PGIMSR from December 2016 to January, 2018. Clearance from institutional ethics committee was taken before the study was started. An informed, bilingual and written consent was obtained from each patient. A total of 100 cases admitted constituted the sample size. The sample size was calculated as follows,

Sample size calculation

It was convenience sampling method where complete enumeration of the sample size was followed taking into consideration as the exact prevalence of congestive cardiac failure was not available, the three year report of population and hospital registry of congestive heart failure 2014 – 2017 where ESI medical College & PGIMSR contributed 87 cases in year 2014. Assuming similar case load and reporting it was expected the sample size to be around 100.

The inclusion and exclusion criteria were as follows,

Inclusion criteria

1. Age between 18-80 yrs.
2. Patient satisfying 2 major or 1 major and 2 minor or 5 minor criteria as per Framingham criteria for heart failure.
3. Patients who are willing to give written, informed consent.

Exclusion criteria

1. Critically ill patients (ICU patients, intubated patients).
2. Any coexisting conditions which can increase CRP levels eg: acute infections, malignancies, recent surgeries, collagen vascular diseases, autoimmune disorders
3. Patients with history of myocardial infarction within 2

months.

4. Presence of bleeding or thrombotic disorders

The data for this study was collected by evaluating the patient in the form of detailed history taking, clinical examination, and relevant investigations for this study. Baseline clinical evaluation, 2D echo screening, C-reactive protein estimation was conducted for all the patients. Patients with CCF were divided into two groups: mild CHF (NYHA class 1&2) and severe (CHF NYHA class 3 & 4) groups. The numeric parameters were expressed as mean +/- SD whereas nonnumeric parameters as frequencies and percentages.

Echocardiography

Echocardiography of all the patients was performed by using commercially available 2D Acuson 2000 echo machine with 2-4 MHz phased array transducer. The Measurements of cardiac dimensions done using M mode echocardiography was taken as per the recommendations of the American Society for Echocardiography.

Images were obtained by four standard transducer positions:

- parasternal,
- apical,
- subcostal, and
- suprasternal

Following echocardiographic parameters were calculated

- E Wave (Early diastolic mitral inflow velocity)
- A Wave (Late diastolic mitral inflow velocity)
- E' velocity (Early diastolic lateral mitral inflow velocity)
- A velocity (Late diastolic lateral mitral annular relaxation velocity)
- E/E' Ratio

- E/A Ratio
- Deceleration time (DT)
- Isovolumic Relaxation Time (IVRT)
- Septal wall thickness
- Left atrial volume index
- Left ventricular end diastolic volume
- Left ventricular end systolic volume
- Left ventricular ejection fraction

Technique of calculating above mentioned parameters

E wave, A wave, Deceleration time (DT): Mitral inflow was recorded from apical four-chamber view. After the proper alignment of the view, the sample volume was positioned at the tips of mitral leaflet. Measurements were recorded at end-expiration and multiple beats was averaged.

Tissue Doppler mitral annular velocity: From the four-chamber apical view, the sample volume was positioned on the annulus, near the insertion site of the mitral valve. Both the septal and lateral sites were recorded. Spectral and velocity gain was lowered. The sweep speed was high between 50 – 100 cm/sec. Measurements of 3 or more consecutive cycles was obtained at end-expiration. The early and late diastolic annular velocity were labelled as e' and a' respectively.

Iso-volumetric relaxation time (IVRT): It was derived using

pulsed Doppler from a modified apical four-chamber view. Image was adjusted to allow simultaneous visualisation of left ventricular inflow and outflow and then sample volume was placed midway between inflow and outflow areas. A large sample volume (3-4 mm) will be taken. IVRT was obtained by measuring the time from middle of aortic closure click to the onset of E wave of mitral flow. Measurements were taken at end expiration and multiple beats were averaged.

Septal wall thickness: Septal wall thickness was measured in end-diastolic phase at the beginning of QRS complex on ECG tracing. Measurements were done in left para- sternal long axis view at the base of the septum from leading edge to leading edge.

Left atrial volume index (LAVI): Left atrial volume was obtained using the bi- planer approach from apical four-chamber view. Left atrial area was measured at end- systole just prior to mitral valve opening. Following formula was used to calculate left atrial volume:

$$\text{Left atrial volume} = (0.85 \times A1 \times A2) \div L$$

Where A1 = area of left atrium by planimetry in apical four-chamber view,

A2 = area of left atrium by planimetry in apical two-chamber view, and L = distance from the mitral annular plane to the superior border of left atrium.

Left Atrial volume index then was calculated by dividing left atrial volume by body surface area.

Left ventricular end-diastolic and end-systolic volume: Left ventricular volumes were measured using the Simpson's method in apical four-chamber and two chamber views. End diastolic volume frame was taken at the beginning of qRS complex on the electrocardiographic tracing and end systolic volume frame were taken at the end of T wave on electrocardiographic tracing.

Left ventricular ejection fraction (LVEF): It was measured by a formula, (LVEF = End-diastolic volume – End-systolic volume ÷ End-diastolic volume) and was expressed as fraction or decimal.

Statistical analysis

The data was obtained in a predesigned proforma specially designed for the purpose. Comparison of the levels of CRP among these 2 groups will be carried out by Mann Whitney U-test/ t-test. Correlation between CRP, LVEF (Left ventricular ejection fraction), LVEDP (Left ventricular end diastolic pressure) and other hemodynamic parameters derived from 2d echo findings were conducted. Wherever the correlation coefficient comes out be strictly significant for those parameters regression analysis was conducted.

Bar diagram and pie charts were drawn to represent the categorized data. P value less than 5% was considered as statistically significant. The data was analysed using statistical package for social services (SPSS vs. 20).

Results

Table 1: Distribution of the study subjects according to NYHA class

NYHA CLASS	Frequency	Percent
Mild (NYHA class 1 & 2)	52	52.0
Severe (NYHA class 3 & 4)	48	48.0
Total	100	100.0

The distribution of the study group according to NYHA class had shown that, about 52% of the study subjects had Mild (NYHA class 1 & 2) of cardiac failure and 48% were classified as severe (NYHA class 3 & 4).

Table 2: Distribution of the study subjects according to age group

Age group	Mild (NYHA class 1 & 2) n (%)	Severe (NYHA class 3 & 4) n (%)	Total n (%)
41 – 50 years	4 (7.7)	9 (18.8)	13 (13.0)
51 – 60 years	23 (44.2)	25 (52.1)	48 (48.0)
61 – 70 years	22 (42.3)	11 (22.9)	33 (33.0)
71 – 80 years	3 (5.8)	3 (6.2)	6 (6.0)
Total	52 (100)	48 (100)	100 (100.0)

X2 Value=5.522 DF=3 p value=0.137, NS

About 44.2% of the patients with mild disease (NYHA class 1 & 2) and 52.1% with severe disease (NYHA class 3 & 4) belonged to 51 – 60 years of age group. This difference in age was not statistically significant between the two groups.

Table 3: Distribution of the study subjects according to sex

Sex	Mild (NYHA class 1 & 2) n (%)	Severe (NYHA class 3 & 4) n (%)	Total n (%)
Male	28 (53.8)	17 (35.4)	45 (45.0)
Female	24 (46.2)	31 (64.6)	55 (55.0)
Total	52 (100)	48 (100)	100 (100.0)

X2 Value=3.425 DF=1 p value=0.064, NS

About 53.8% of the patients with mild disease (NYHA class 1 & 2) were males and 64.6% of the patients with severe disease (NYHA class 3 & 4) were females. There was no statistically significant difference in sex between the two groups.

Table 4: Distribution of the study subjects according to history of hypertension

H/O Hypertension	Mild (NYHA class 1 & 2) n (%)	Severe (NYHA class 3 & 4) n (%)	Total n (%)
Known hypertensive	36 (69.2)	37 (77.1)	73 (73.0)
Not a known hypertensive	16 (30.8)	11 (22.9)	27 (27.0)
Total	52 (100)	48 (100)	100 (100.0)

X2 Value=0.781 DF=1 p value=0.377, NS

About 69.2% of the patients with mild disease (NYHA class 1 & 2) and 77.1% with the severe disease (NYHA class 3 & 4) were known hypertensives. This difference in occurrence of hypertension was not statistically significant.

Table 5: Distribution of the study subjects according to palpitation

Palpitation	Mild (NYHA class 1 & 2) n (%)	Severe (NYHA class 3 & 4) n (%)	Total n (%)
Present	11 (21.2)	9 (18.8)	20 (20.0)
Absent	41 (78.8)	39 (81.2)	80 (80.0)
Total	52 (100)	48 (100)	100 (100.0)

X2 Value=0.09 DF=1 p value=0.764, NS

Palpitation was present in 21.2% of the patients with mild disease (NYHA class 1 & 2) and 18.8% of the severe disease (NYHA

Class 3 & 4). This difference in occurrence of palpitation was not statistically significant.

Table 6: Distribution of the study subjects according to difficulty in breathing

Difficulty in breathing	Mild (NYHA class 1 & 2) n (%)	Severe (NYHA class 3 & 4) n (%)	Total n (%)
Present	11 (21.2)	8 (16.7)	19 (19.0)
Absent	41 (78.8)	40 (83.3)	81 (81.0)
Total	52 (100)	48 (100)	100 (100.0)

X2 Value=0.327 DF=1 p value=0.568, NS

Difficulty in breathing was present in 21.2% of the patients with mild disease and 16.7% of the patients with severe disease (NYHA class 3 & 4). This difference was also statistically not significant.

Table 7: Distribution of the study subjects according to Tiredness

Tiredness	Mild (NYHA class 1 & 2) n (%)	Severe (NYHA class 3 & 4) n (%)	Total n (%)
Present	31 (59.6)	24 (50.0)	55 (55.0)
Absent	21 (40.4)	24 (50.0)	45 (45.0)
Total	52 (100)	48 (100)	100 (100.0)

X2 Value=0.932 DF=1 p value=0.334, NS

Tiredness was present in 59.6% of the patients with mild disease (NYHA class 1 & 2) and 50% of the patients with severe disease (NYHA class 3 & 4). This difference was also statistically not significant.

Table 8: Distribution of the study subjects according to swelling of lower limbs

Swelling of LL	Mild (NYHA class 1 & 2) n (%)	Severe (NYHA class 3 & 4) n (%)	Total n (%)
Present	27 (51.9)	26 (54.2)	53 (53.0)
Absent	25 (48.1)	22 (45.8)	47 (47.0)
Total	52 (100)	48 (100)	100 (100.0)

X2 Value=0.05 DF=1 p value=0.822, NS C

Swelling of the lower limbs was present in 51.9% of the patients with mild disease (NYHA class 1 & 2) and 54.2% of the patients with severe disease (NYHA class 3 & 4). This difference in swelling of the limbs was not statistically significant.

Table 9: Distribution of the study subjects according to paroxysmal nocturnal dyspnea

PND	Mild (NYHA class 1 & 2) n (%)	Severe (NYHA class 3 & 4) n (%)	Total n (%)
Present	9 (17.3)	7 (14.6)	16 (16.0)
Absent	43 (82.7)	41 (85.4)	84 (84.0)
Total	52 (100)	48 (100)	100 (100.0)

X2 Value=0.138 DF=1 p value=0.71, NS

About 17.3% of the patients with mild disease (NYHA class 1 & 2) and 14.6% with the severe disease (NYHA class 3 & 4) had paroxysmal nocturnal dyspnea. This difference in occurrence of paroxysmal nocturnal dyspnea was not statistically significant.

Table 10: Distribution of the study subjects according to cough at night

Cough at night	Mild (NYHA class 1 & 2) n (%)	Severe (NYHA class 3 & 4) n (%)	Total n (%)
Present	9 (17.3)	7 (14.6)	16 (16.0)
Absent	43 (82.7)	41 (85.4)	84 (84.0)
Total	52 (100)	48 (100)	100 (100.0)

X2 Value=0.138 DF=1 p value=0.71, NS

The cough at night was present in 17.3% of the mild diseases (NYHA class 1 & 2) and 14.6% of the severe disease (NYHA class 3 & 4). This difference in cough at night was not statistically significant.

Table 11: Distribution of the study subjects according to breathlessness on lying down

Breathlessness	Mild (NYHA class 1 & 2) n (%)	Severe (NYHA class 3 & 4) n (%)	Total n (%)
Present	12 (23.1)	7 (14.6)	19 (19.0)
Absent	40 (76.9)	41 (85.4)	81 (81.0)
Total	52 (100)	48 (100)	100 (100.0)

X2 Value=1.17 DF=1 p value=0.279, NS

Down

Breathlessness was present in 23.1% of the patients with mild disease (NYHA class 1 & 2) and 14.6% of the patients with severe disease (NYHA class 3 & 4). This difference was not statistically significant between the patients with mild and severe disease.

Table 12: Distribution of the study subjects according to body mass index

BMI	Mild (NYHA class 1 & 2)	Severe (NYHA class 3 & 4)	T value	P value, Sig
Mean ± SD	29.89 ± 3.9	29.33 ± 3.7	0.731	0.467, NS

The mean (± SD) BMI of patients with mild disease was 29.89 (± 3.9) and among the severe disease patients was 29.33. This difference in BMI was not statistically significant.

Table 16: Distribution of the study subjects according to ECHO Parameters

ECHO parameters	Mild (NYHA class 1 & 2)	Severe (NYHA class 3 & 4)	T value	P value, Sig
E	7.45 ± 1.03	7.36 ± 0.94	0.441	0.66, NS
A	9.54 ± 1.13	9.67 ± 1.16	0.596	0.552, NS
S	6.3 ± 1.18	6.44 ± 1.41	0.506	0.614, NS
E/E'	10.14 ± 1.07	9.99 ± 1.11	0.674	0.502, NS
E/A	1.0 ± 0.26	1.04 ± 0.26	0.719	0.474, NS
Deceleration	215.81 ± 15.87	216.92 ± 16.59	0.342	0.733, NS
Isovolumetric relaxation time (ms)	105.79 ± 11.2	104.33 ± 10.04	0.682	0.497, NS
Septal wall thickness (cm)	0.95 ± 0.08	0.96 ± 0.11	0.022	0.983, NS
Left ventricular mass index (g/m2)	69.18 ± 10.27	70.52 ± 11.24	0.624	0.534, NS
Left atrial volume index (mL/m2)	32.25 ± 3.91	31.12 ± 4.16	1.402	0.164, NS
Left ventricular end diastolic volume (mL)	88.16 ± 5.63	88.51 ± 4.98	0.323	0.747, NS
Left ventricular end systolic volume (mL)	38.68 ± 4.42	38.85 ± 4.19	0.196	0.845, NS
Ejection fraction (%)	54.5 ± 4.1	55.1 ± 4.29	0.695	0.489, NS

In mild disease group (NYHA class 1 & 2), the mean E was 7.45 (± 1.03), A was 9.54 (± 1.13), S was 6.3 (± 1.18), E/E' ratio was 10.14 (± 1.07), E/A ratio was 1.0 (± 0.26), deceleration as 215.81 (± 15.87), Isovolumetric

Table 13: Distribution of the study subjects according to past history of diabetes mellitus

Past history diabetes mellitus	Mild (NYHA class 1 & 2) n (%)	Severe (NYHA class 3 & 4) n (%)	Total n (%)
Present	19 (36.5)	19 (39.6)	38 (38.0)
Absent	33 (63.5)	29 (60.4)	62 (62.0)
Total	52 (100)	48 (100)	100 (100.0)

X2 Value=0.932 DF=1 p value=0.334, NS

About 36.5% of the patients with mild disease (NYHA class 1 & 2) and 39.6% with severe disease (NYHA class 3 & 4) had no statistically significant difference in past history of diabetes.

Table 14: Distribution of the study subjects according to past history of hyperlipidemia

Past history hyperlipidemia	Mild (NYHA class 1 & 2) n (%)	Severe (NYHA class 3 & 4) n (%)	Total n (%)
Present	20 (38.5)	23 (47.9)	43 (43.0)
Absent	32 (61.5)	25 (52.1)	57 (57.0)
Total	52 (100)	48 (100)	100 (100.0)

X2 Value=0.91 DF=1 p value=0.34, NS

Past history of hyperlipidemia was present in 38.5% of the patients with mild disease (NYHA class 1 & 2) and 47.9% with severe disease (NYHA class 3 & 4). This difference in past history of hyperlipidemia was not statistically significant.

Table 15: Distribution of the study subjects according to past history of CHD

Past history CHD	Mild (NYHA class 1 & 2) n (%)	Severe (NYHA class 3 & 4) n (%)	Total n (%)
Present	21 (40.4)	16 (33.3)	37 (37.0)
Absent	31 (59.6)	32 (66.7)	63 (63.0)
Total	52 (100)	48 (100)	100 (100.0)

X2 Value=0.532 DF=1 p value=0.466, NS

Past history of CHD was present in 40.4% of the patients with mild (NYHA class 1 & 2) and severe disease (NYHA class 3 & 4). There was no statistically significant in the past history of CHD between the mild and severe disease.

relaxation time (ms) 105.79 (± 11.2), Septal wall thickness was 0.95 (± 0.08) cms, Left ventricular mass index was 69.18 g/m2 (± 10.27), left atrial volume index was 32.25 mL/m2 (± 3.91), left ventricular end systolic volume was 38.68 mL and

Ejection fraction was 54.5 % (\pm 15.2). Among the patients with severe disease (NYHA class 3 & 4), E was 7.36 (\pm 0.94), A was 9.67 (\pm 1.16), S was 6.44 (\pm 1.41), E/E' ratio was 9.99 (\pm 1.11), E/A ratio was 1.04 (\pm 0.26), Deceleration was 216.92 (\pm 16.59), Isovolumetric relaxation time was 104.33 (\pm 10.04) ms, Septal wall thickness was 0.96 (\pm 0.11) cms, left ventricular mass index was 70.52 (\pm 11.24) g/m², left atrial volume index was 31.12 (\pm 4.16), left ventricular end diastolic volume was 88.51 mL (\pm 4.98), left ventricular end systolic volume was 38.85 (\pm 4.19) mL and Ejection fraction was 55.08% (\pm 12.24). There was no statistically significant difference in any of these parameters between mild and severe disease.

Table 17: Distribution of the study subjects according to C reactive protein levels

C reactive protein	Mild (NYHA class 1 & 2)	Severe (NYHA class 3 & 4)	T value	P value, Sig
Mean \pm SD	4.86 \pm 1.84	4.54 \pm 1.98	0.845	0.4, NS

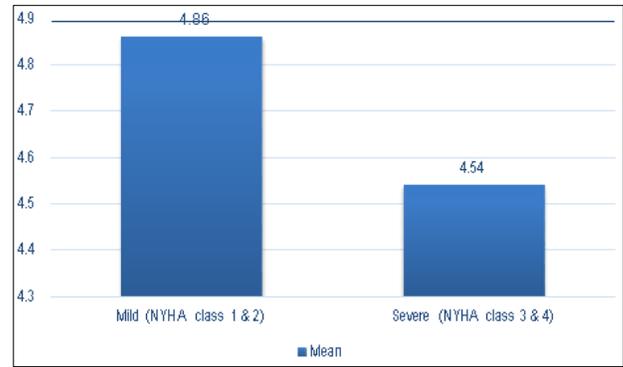


Chart 16: Distribution of the study subjects according to C reactive protein levels

The mean (\pm SD) C reactive protein levels in patients with mild disease (NYHA 1 & 2) was 4.86 mg/L and 4.54 mg/L in the patients with severe disease (NYHA class 3 & 4). This difference in C reactive proteins levels was not statistically significant between the patients of mild and severe disease.

Table 18: Correlation of C reactive protein levels with CRP according to NYHA class

ECHO parameters	Mild (NYHA 1 & 2) CRP (r)	Severe (NYHA 1 & 2) CRP (r)
E	0.14	0.093
A	-0.087	-0.081
S	0.349*	-0.531*
E/E'	0.210	-0.316*
E/A	-0.025	-0.014
Deceleration	0.236	-0.043
Isovolumetric relaxation time (ms)	-0.312*	-0.192
Septal wall thickness (cm)	-0.185	-0.044
Left ventricular mass index (g/m ²)	-0.063	-0.063
Left atrial volume index (mL/m ²)	-0.076	0.183
Left ventricular end diastolic volume (mL)	0.113	-0.205
Left ventricular end systolic volume (mL)	-0.282*	-0.137
Ejection fraction (%)	0.204	-0.052

The patients with mild disease (NYHA class 1 & 2), the correlation coefficient of E was 0.14, A was -0.087, S was 0.349, E/E' was 0.21, E/A was -0.025, Deceleration was 0.236, isovolumetric relaxation time (ms) was 0.312, septal wall thickness was -0.185, left ventricular mass index (g/m²) was -0.063, left atrial volume index was -0.076, left ventricular end diastolic volume was 0.113, left ventricular end systolic volume was -0.282 and ejection fraction was 0.204.

In patients with severe disease, the correlation coefficient of E was 0.093, A was -0.081, S was -0.531, E/E' was 0.316, E/A was -0.014, Deceleration was -0.043, isovolumetric relaxation time (ms) was -0.192, septal wall thickness was -0.044, left ventricular mass index (g/m²) was -0.063, left atrial volume index was 0.183, left ventricular end diastolic volume was -0.205, left ventricular end systolic volume was -0.137 and ejection fraction was -0.052.

S had positive and significant correlation and isovolumetric relaxation time had negative and significant correlation time in mild disease patients. In patients with severe disease, S and E/E' was had negative and statistically significant correlation.

Discussion

Congestive Cardiac Failure (CCF) is a major problem affecting millions of people yearly and carries a high mortality. It is a complex syndrome characterized by shortness of breath, fatigue, congestion and cachexia and symptoms related to inadequate tissue perfusion, fluid retention and neurohormonal activation. HF is a burgeoning problem worldwide, with more than 20 million people affected. The overall prevalence of HF in the adult population in developed countries is 2%. HF prevalence follows an exponential pattern, rising with age, and affects 6- 10% of people over age 65.3

The inflammatory marker that presently seems most suitable to assess inflammation is CRP.10 Cytokines such as tumour necrosis factor alpha (TNF - α) and interleukin - 6 are significantly elevated, producing negative inotropic effects on the heart and the levels of these cytokines may be negatively associated with prognosis.11

C reactive protein (CRP) has been shown to be associated with an increased risk of various cardiovascular diseases.12 The serum concentration of CRP is also elevated in patients with congestive

Heart failure (CHF).¹³ A study reported that increased CRP was an independent predictor of incident CHF in a community based elderly population.¹⁴

The mildly elevated CRP concentrations in these patients fall well within the range found in healthy subjects, and the standard clinical assays for CRP lack sensitivity within the low-normal range: thus they cannot be used effectively for cardiovascular risk prediction. Since high-sensitivity commercial assays for CRP are now available and it can be hypothesized that measurement of CRP might provide prognostic information in these patients.¹⁵

A cross sectional study was undertaken among the patients between 18-80 years with congestive cardiac failure who were admitted at ESIC MEDICAL COLLEGE & PGIMS from December 2016 to June 2018. A total of 100 cases admitted constituted the sample size.

NYHA class of disease

This study had shown that, 52% of the study subjects had Mild (NYHA class 1 & 2) of cardiac failure and 48% were classified as severe disease (NYHA class 3 & 4). In a study by Huang *et al*, 44% of the cases had NYHA class II disease, 33% had NYHA class III and 22% had NYHA class IV.¹⁶ In a study by Ansari *et al*, 40.63% of the patients had mild CHF (NYHA class I & II) and 59.37% of the patients had severe CHF (NYHA class III & IV).¹

Age group

Most of the study subjects in this study belonged to belonged to 51 – 60 years of age group. In a study by Huang *et al*, the mean age group was 61 years.¹⁶ In a study by Ansari *et al*, the mean age of mild CHF patients was 52.77 years and in severe CHF patients was 57.74 years.¹ In a study by DuBrock *et al*, the mean age of the patients with normal CRP values was 70 years and high CRP values was 67 years.¹⁷

Sex

About 53.8% of the patients with mild disease (NYHA class 1 & 2) were males and 64.6% of the patients with severe disease (NYHA class 3 & 4) were females as shown by this study. Huang *et al* reported that 67% of the cases were males in contradiction to this disease.¹⁶ In a study by Ansari *et al*, about 69.23% of the patients with mild CHF and 68.42% of the severe CHF patients were males.¹ In a study by DuBrock *et al*, about 46.2% in normal CRP and 49.6% of the high CRP group were males.¹⁷

History of hypertension

About 69.2% of the patients with mild disease (NYHA class 1 & 2) and 77.1% with the severe disease (NYHA class 3 & 4) had history of hypertension. In a study by DuBrock *et al*, about 83.9% of the normal CRP patients and 85.1% of the high CRP patients had hypertension.¹⁷

Clinical features

Palpitation was present in 21.2% of the patients with mild disease (NYHA class 1 & 2) and 18.8% of the severe disease (NYHA class 3 & 4). Difficulty in breathing was present in 21.2% of the patients with mild disease and 16.7% of the patients with severe disease (NYHA class 3 & 4). Tiredness was present in 59.6% of the patients with mild disease (NYHA class 1 & 2) and 50% of

the patients with severe disease (NYHA class 3 & 4). Swelling of the lower limbs was present in 51.9% of the patients with mild disease (NYHA class 1 & 2) and 54.2% of the patients with severe disease (NYHA class 3 & 4). About 17.3% of the patients with mild disease (NYHA class 1 & 2) and 14.6% with the severe disease (NYHA class 3 & 4) had paroxysmal nocturnal dyspnea. The cough at night was present in 17.3% of the mild diseases (NYHA class 1 & 2) and 14.6% of the severe disease (NYHA class 3 & 4). Breathlessness on lying down was present in 23.1% of the patients with mild disease (NYHA class 1 & 2) and 14.6% of the patients with severe disease (NYHA class 3 & 4). In a study by DuBrock *et al*, about 15.1% of the patients with normal CRP and 24.8% with high CRP had moderate or severe edema.¹⁷

Body mass index

The mean (\pm SD) BMI of patients with mild disease was 29.89 (\pm 3.9) and among the severe disease patients was 29.33. In a study by Ansari *et al*, the mean BMI in mild CHF was 23.87 and 21.74 among the severe CHF patients.¹ DuBrock *et al* reported that the BMI in patients with normal CRP was 32.1 and 35.1 in patients with high CRP.¹⁷

Past history of diseases

About 36.5% of the patients with mild disease (NYHA class 1 & 2) and 39.6% with severe disease (NYHA class 3 & 4) had past history of diabetes mellitus. Past history of hyperlipidemia was present in 38.5% of the patients with mild disease (NYHA class 1 & 2) and 47.9% with severe disease (NYHA class 3 & 4). Past history of CHD was present in 40.4% of the patients with mild (NYHA class 1 & 2) and severe disease (NYHA class 3 & 4). DuBrock *et al* reported that 37.6% of the patients with normal CRP and 38.8% with high CRP had ischemic heart disease and 36.6% of the patients had normal CRP and 47.9% with high CRP patients had diabetes mellitus.¹⁷

ECHO parameters

In mild disease group (NYHA class the patients with mild disease (NYHA class 1 & 2), the correlation coefficient of E was 0.14, A was -0.087, S was 0.349, E/E' was 0.21, E/A was -0.025, Deceleration was 0.236, isovolumetric relaxation time (ms) was 0.312, septal wall thickness was -0.185, left ventricular mass index (g/m²) was -0.063, left atrial volume index was -0.076, left ventricular end diastolic volume was 0.113, left ventricular end systolic volume was -0.282 and ejection fraction was 0.204.

In patients with severe disease, the correlation coefficient of E was 0.093, A was -0.081, S was -0.531, E/E' was 0.316, E/A was -0.014, Deceleration was -0.043, isovolumetric relaxation time (ms) was -0.192, septal wall thickness was -0.044, left ventricular mass index (g/m²) was -0.063, left atrial volume index was 0.183, left ventricular end diastolic volume was -0.205, left ventricular end systolic volume was -

0.137 And ejection fraction was -0.052. In a study by Huang *et al*, the mean cardiac index was 2.0 L/min/M² in patients without MACE and 2.1 L/min/M² in patients with MACE. The mean left ventricular end diastolic pressure was 21 mm Hg in non-MACE patients and 28 mm Hg in MACE patients.¹⁶ In a study by Ansari *et al*, the mean left ventricular ejection fraction was 37.7 in mild CHF and 20.92 in severe CHF patients.¹

C reactive protein levels

The mean (\pm SD) C reactive protein levels in patients with mild disease (NYHA 1 & 2) was 4.86 mg/L and 4.54 mg/L in the patients with severe disease (NYHA class 3 & 4). This difference in C reactive proteins levels was not statistically significant between the patients of mild and severe disease. In a study by Huang *et al*, the mean C reactive protein level among the patients without MACE was 3.12 mg/L and 5.76 mg/L in patients with MACE.¹⁶ In a study by Ansari *et al*, the mean CRP levels in CHF patients was 4.35 mg/L.

Correlation of CRP with ECHO parameters

S had positive and significant correlation and isovolumetric relaxation time had negative and significant correlation time in mild disease patients. In patients with severe disease, S and E/E' was had negative and statistically significant correlation. In a study by Huang *et al*, the concentrations of CRP were significantly higher in CHF patients than 16 healthy controls and increased with the severity of CHF especially in the severe (NYHA class III or IV) group.¹⁶ In a study by Ansari *et al*, the correlation coefficients of the patients with left ventricular ejection fraction was 0.08.¹

Conclusion

This study was mainly undertaken to study the CRP levels and its prognostic importance in heart failure patients. This study had shown that most of the heart failure patients were aged above 50 years, males, with patients having comorbidities. The CRP had correlation with some echocardiographic parameters. This study had shown that CRP is an important prognostic marker in chronic heart failure. But this study is not without limitations. This is the cross sectional study which has weakness by the methodology itself. The sample size was not calculated and any sampling methods were not followed. But this study was able to bring out many important facts about use of CRP in diagnosis of chronic heart failure. Further research in this direction is important to study the CRP as an important prognostic factor of chronic heart failure.

Summary

- Congestive Cardiac Failure (CCF) is a major problem affecting millions of people yearly and carries a high mortality.
- C reactive protein (CRP) has been shown to be associated with an increased risk of various cardiovascular diseases.
- A cross sectional study was undertaken among the patients between 18-80 years with congestive cardiac failure who were admitted at ESIC MEDICAL COLLEGE & PGIMSR
- About 52% of the study subjects had Mild (NYHA class 1 & 2) of cardiac failure and 48% were classified as severe disease (NYHA class 3 & 4).
- Most of the study subjects in this study belonged to 51 – 60 years of age group.
- About 53.8% of the patients with mild disease (NYHA class 1 & 2) were males and 64.6% of the patients with severe disease (NYHA class 3 & 4) were females as shown by this study.
- About 69.2% of the patients with mild disease (NYHA class 1 & 2) and 77.1% with the severe disease (NYHA class 3 &

4) had history of hypertension.

- Palpitation was present in 21.2% of the patients with mild disease (NYHA class 1 & 2) and 18.8% of the severe disease (NYHA class 3 & 4).
- Difficulty in breathing was present in 21.2% of the patients with mild disease and 16.7% of the patients with severe disease (NYHA class 3 & 4).
- Tiredness was present in 59.6% of the patients with mild disease (NYHA class 1 & 2) and 50% of the patients with severe disease (NYHA class 3 & 4).
- Swelling of the lower limbs was present in 51.9% of the patients with mild disease (NYHA class 1 & 2) and 54.2% of the patients with severe disease (NYHA class 3 & 4).
- About 17.3% of the patients with mild disease (NYHA class 1 & 2) and 14.6% with the severe disease (NYHA class 3 & 4) had paroxysmal nocturnal dyspnea.
- The cough at night was present in 17.3% of the mild diseases (NYHA class 1 & 2) and 14.6% of the severe disease (NYHA class 3 & 4).
- Breathlessness was present in 23.1% of the patients with mild disease (NYHA class 1 & 2) and 14.6% of the patients with severe disease (NYHA class 3 & 4).
- The mean (\pm SD) BMI of patients with mild disease was 29.89 (\pm 3.9) and among the severe disease patients was 29.33.
- About 36.5% of the patients with mild disease (NYHA class 1 & 2) and 39.6% with severe disease (NYHA class 3 & 4) had past history of diabetes mellitus.
- Past history of hyperlipidemia was present in 38.5% of the patients with mild disease (NYHA class 1 & 2) and 47.9% with severe disease (NYHA class 3 & 4).
- Past history of CHD was present in 40.4% of the patients with mild (NYHA class 1 & 2) and severe disease (NYHA class 3 & 4).

In mild disease group (NYHA class The patients with mild disease (NYHA class 1 & 2), the correlation coefficient of E was 0.14, A was -0.087, S was 0.349, E/E' was 0.21, E/A was -0.025, Deceleration was 0.236, isovolumetric relaxation time (ms) was 0.312, septal wall thickness was -0.185, left ventricular mass index (g/m²) was -0.063, left atrial volume index was -0.076, left ventricular end diastolic volume was 0.113, left ventricular end systolic volume was -0.282 and ejection fraction was 0.204.

- In patients with severe disease, the correlation coefficient of E was 0.093, A was -0.081, S was -0.531, E/E' was 0.316, E/A was -0.014, Deceleration was -0.043, isovolumetric relaxation time (ms) was -0.192, septal wall thickness was -0.044, left ventricular mass index (g/m²) was -0.063, left atrial volume index was 0.183, left ventricular end diastolic volume was -0.205, left ventricular end systolic volume was -0.137 and ejection fraction was -0.502.
- The mean (\pm SD) C reactive protein levels in patients with mild disease (NYHA 1 & 2) was 4.86 mg/L and 4.54 mg/L in the patients with severe disease (NYHA class 3 & 4).
- S had positive and significant correlation and isovolumetric relaxation time had negative and significant correlation time in mild disease patients. In patients with severe disease, S and E/E' was had negative and statistically significant correlation.

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