ORIGINAL ARTICLE

The Role of Inflammation in Patients with Chronic Heart Failure

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ABSTRACT

Aims: To investigate the contributory role of Inflammation in the genesis of Heart Failure in the hospitalized patients of Arar, K.S.A and thereby strengthen the knowledge of Medical fraternity with regards to mechanism of Cardiac Failure
Study design-Hospital Based Cross Sectional Study
Place of study-The study was conducted in Prince Abdullah Bin musaed cardiac centre Arar, K.S.A
Methods -The sample study included 50 cases in which inflammatory markers[CRP,CBP,ESR] where studied by collection of values of patients with chronic
Heart failure from hospital records and analyzed by comparing their pre-treatment and post treatment levels by Spss16.0[Paired T Test]
Results- Study showed the observation of significant P value[<0.05] for CRP,PLR,ESR With following values
1. CRP[P-<0.05],Mean[13.99 and 1.68],[S.D-11.15 and 6.0]
2. TLC-[P->0.05],Mean[12155 and 12100],S.D[11030 and 14163]
3. PLR[P<0.05],Mean[119 and 130] S.D[22.20 and 27.28]
4. ESR[P<0.05] Mean[11.04 and 5.32] S.D[17.06 and 5.15]
Conclusion: In view of the significant P value[<0.05] for CRP, PLR,ESR, suggestions can be made for these markers to be used in Patients with Chronic Heart Failure
Key Words: Inflammation ,Cardiac failure, Inflammatory Markers, Study, HTN[Hypertension],CKD[Chronic Kidney Disease],MI[Myocardial Infarction],HF[Heart Failure],AF[Atrial Fibrillation],SVT[Supra Ventricular Tachycardia]

INTRODUCTION

Chronic Heart failure is one of the common medical conditions affecting the community in general. Current Literature suggests the very key role of Life style for the origin of this disease along with other contributing factors. Chronic Heart Failure can be associated with Inflammation[1].The role of Inflammation in Chronic Heart failure patients can be exemplified by the fact that Inflammatory markers are raised in patients with decompensated phase of Chronic Heart Failure[2].During recovery phase of disease the markers are decreased[2].Studies have linked the markers of inflammation with prognosis of disease[3]. Literature also suggest the association of severity of disease with levels of inflammatory markers[4]. Inflammation contributes to development of Heart failure due to the fact that it hastens the underlying risk factors of Heart Failure like Atherosclerosis ,Diabetes Mellitus among others[5].It was also observed that there is elevated levels of cytokines like TNF, IL-1 β& IL-6 which are all proinflammatory in nature in patients with Heart Failure[6]. The role of Inflammation is further proved by the observation of the findings of increased occurrence of disease in inflammatory state like Rheumatoid Arthrits[7].In addition relation between cytokine levels and Heart Failure is noted in studies along with their significant prognostic value[8]. Experimental studies showed the therapeutic implications of inflammatory cytokines in Heart Failure[9].Potential Biomarkers for Patients with Heart Failure are available in the form of various inflammatory substances like IL-6,IL-10 and CRP[10].

MATERIALS AND METHODS

Fifty Patients who were diagnosed with Chronic Heart Failure based on Clinical, Echocardiography and Electrocardiogram [ECG] findings are selected for study and the Values of Markers of Inflammation such as a.CRP b.CBP.c.ESR of these patients are noted from Hospital records before and after treatment for Acute decompensation[Acute Heart Failure]phase and thereby analyze these markers and correlate with disease. These patients are free from conditions like Infection, Inflammation and Malignancy, which can influence the values of a.CRP b.CBP c.ESR. Under Complete Blood Picture [CBP] category two Parameters are chosen. These are Total Leukocyte Count [TLC] and Platelet to Lymphocyte Ratio[PLR].Proforma for entry of study variables is prepared for data entry and data is subjected to soft ware SPSS-16.0 for analysis by Paired T test[statistical],there by
furnishing the results of study.

RESULTS

The study showed Mean &Standard Deviation values of C-reactive Protein as 13.99[+/-11.15] and 1.68[+/-6.0],for Total Leukocyte count as 12155[+/-11030] and12100[+/-14163]and Platelet to Lymphocyte ratio 119[+/-22.20] and 130 [+/-27.28].The Values of Erythrocyte Sedimentation rate are 11.04[+/-17.06]and 5.32[+/-5.15] before and after treatment respectively. The P values for CRP is 0.00[<0.05],forTLC its 0.91[>0.05] ,for PLR it is 0.046[<0.05] and for ESR its 0.018[<0.05].

The causes of Chronic Heart Failure in present study include 1.Ischemic [56%] 2.Rhythm disorders[8%] 3.Chronic Kidney Disease [8%] 4. Thyroid disease [8%] 5.Hypertension[6%], 6. Cardiomyopathy [6%] 7.Inflammatory Heart Disease [4%] 8.Valvular Heart Disease[4%]

DISCUSSION

Chronic Heart Failure is a complex multi step disease with varied etiologies and many Pathogenetic Mechanisms, which include Haemodynamic, Immunological/ Inflammatory and Coagulation abnormalities along with Haematological changes that predispose to the Condition. There is also definite role for Neurohormonal mechanisms. The role of Inflammation in Cardiac Failure is proven in many studies due to the fact that CRP is raised which is marker of Inflammation. C-reactive Protein leads to induction of Adhesion molecules in injured Cardiac tissue ,with consequent recruitment and activation of Monocytes[M2 sub type] that are responsible for Cardiac Remodelling. Evidence for Monocyte activation is shown by increased Neopterin [marker of Monocyte activation],which also correlated with raised TNF-alpha, another marker of Inflammation[11].Stimulation of Neurohormonal pathway in patients with Cardiac failure happens to maintain Cardiac output initially by increased Cardiac contractility and Sodium/water retention but later can exert adverse effects on Cardiovascular System[Apoptosis] ,as shown by clinical improvement in Heart failure patients by use of Neurohormonal antagonists[Adrenergic and Angiotensin Inhibitors][12].Haemodynamic model for Cardiac failure is best seen in patients with Chronic Kidney Disease who develops Chronic Heart Failure, wherein elevated preload and afterload due to hypervolemia and hypertension can induce compensatory Cardiac remodelling in the form of Left ventricular hypertrophy ,which maintains cardiac function[13].Studies have shown the relation of Erythrocyte Sedimentation Rate [ESR] with severity of disease in Heart Failure Patients ,which also correlated with Fibrinogen levels[14].Literature also proved that Fibrinogen levels were higher in patients with Heart Failure in relation to Control subset, and levels also correlated with severity of Heart Failure[15].Platelet to Lymphocyte ratio[PLR] is a new marker of Inflammation. High PLR[›110] with significant p-value[‹0.05]has shown poor prognosis in Heart Failure Patients in some studies due to fact that it may initiate Inflammatory response[16].These findings also matched the findings of current study.[p‹0.046].Angiogenin can serve as marker of Cardiac remodelling due to its role in Angiogensesis[17].IL-6 represents marker of Heart Failure in acute post ischemic phase ,which can be potential therapeutic target[18].ANP/BNP[Atrial and Brain Natriuretic peptides] serve as markers of heart wall strain and useful for both diagnosis and for treatment monitoring[19].Studies have suggested Galectin-3 and Soluble suppression of tumorigenecity -2[Gal-3,Sst2] as markers of Cardiac Fibrosis,which were investigated but not proved still[20].Prognostic value of raised Total Leukocyte count in patients is reported ,to correlate with high hospitalization rate ,with significant P value[‹0.05],which is in contrast to present study[P value-›0.05][21].The prognosis and outcome of Heart Failure depends on type of Heart Failure ,that is Acute Heart Failure or Chronic Heart Failure. Acute Heart

Failure is defined as episodic symptomatic deterioration, while Chronic Heart Failure is defined as patient having heart failure for some time and now free of symptoms for more than a month, with a one year survival of 55-65% and 80-90% respectively[22]. General poor prognostic indicators are decreased Ejection Fraction[EF]

Rhythm disorders, Kidney impairment and less Functional status[23].Primary prevention strategy for Chronic Heart Failure in Community can include maintenance of Healthy Life Style by adoption of Well Balanced Diet, Regular Exercise and avoidance of Stress along with Smoking cessation, which can prevent

Life Style Diseases, like Hypertension,Coronary Heart Disease and Diabetes Mellitus, leading to overall Control of Chronic Heart Failure[24].Studies have shown the beneficial effect of Exercise in patients with Chronic Heart Failure by improving their function status[25].

CONCLUSION

This study is an attempt to find readily available, inexpensive and reliable markers of Chronic Heart failure .The results of study reveals the significance of CRP, Platelet to Lymphocyte ratio[PLR] and ESR with P values of less than 0.05 ,which suggests them to be used as markers of diagnostic , prognostic utility and to monitor treatment response in patients with Chronic Heart Failure. Our Findings Correlated with findings from other studies.

REFERENCES

1. Libby P, Nahrendorf M, Swirski FK. Leukocytes link local and systemic inflammation in ischemic cardiovascular disease: an expanded "cardiovascular continuum". J Am CollCardiol. 2016;67:1091–103..
2. Dick SA, Epelman S. Chronic heart failure and inflammation: what do we really know? Circ Res. 2016;119:159–176.:
3. Anand IS, Latini R, Florea VG, et al. C-reactive protein in heart failure: prognostic value and the effect of valsartan. Circulation. 2005;112:1428–34
4. Tsutamoto T, Hisanaga T, Wada A, et al. Interleukin-6 spillover in the peripheral circulation increases with the severity of heart failure, and the high plasma level of interleukin-6 is an important prognostic predictor in patients with congestive heart failure. J Am CollCardiol. 1998;31:391–8.
5. Libby P, Hansson GK. Inflammation and immunity in diseases of the arterial tree: players and layers. Circ Res. 2015;116:307–11.
6. Mann DL. Innate immunity and the failing heart: the cytokine hypothesis revisited. Circ Res. 2015;116:1254–1268.
7. Sophie Van Linthout· Carsten Tschöpe·Inflammation – Cause or Consequence of Heart Failure or Both? Curr Heart Fail Rep (2017) 14:251–265
8. Torre-Amione G, Kapadia S, Benedict C, Oral H, Young JB, Mann DL. Proinflammatory cytokine levels in patients with depressed left ventricular ejection fraction: a report from the Studies of Left Ventricular Dysfunction (SOLVD). J Am Coll Cardiol. 1996;27:1201–6
9. Westermann D, Van Linthout S, Dhayat S, Dhayat N, Schmidt A, Noutsias M, et al. Tumor necrosis factor-alpha antagonism protects from myocardial inflammation and fibrosis in experimental diabetic cardiomyopathy. Basic Res Cardiol. 2007;102:500–7.
10. Margarita Kunin, Vered Carmon, Michael Arad, Nomy Levin-Iaina, Dov Freimark, Eli J. Holtzman, and Dganit Dinour. Inflammatory Biomarkers in Refractory Congestive Heart Failure Patients Treated with Peritoneal Dialysis. BioMed Research International.2015.1-8
11. Wrigley BJ, Lip GYH, Shantsila E (2015) The role of monocytes and inflammation in the pathophysiology of heart failure. Eur J Heart Fail 13:1161–1171.

12. Justin Hartupee, Douglas L. Mann Neurohormonal activation in heart failure with reduced ejection fraction Nat Rev Cardiol. 2017 January ; 14(1): 30–38
13. Liviu Segall, Ionut Nistor, and Adrian Covic Heart Failure in Patients with Chronic Kidney Disease: A Systematic Integrative Review BioMed Research International Volume 2014, Article ID 937398, 21 pages.
14. Howard l. Haber, Jeffrey A. Leavy, Paul D. Kessler, Marrick l. Kukin, Stephen S. Gottlieb, Milton Packer. The erythrocyte sedimentation rate in congestive heart failure. The New England Journal of Medicine feb. 7, 1991.vol 324.no.6
15. Aušra Mongirdienė, Lolita Kuršvietienė, Artūras Kašauskas. The coagulation system changes in patients with chronic heart failure Medicina (Kaunas) 2010;46(9):642-7
16. Gui-lian Ye, Qiang Chen, Xueyu Chen, Ying-ying Liu, Ting-ting Yin, Qing-he Meng, Yingchao Liu2, Huai-qing Wei2 & Qing-hua Zhou The prognostic role of platelet-tolymphocyte ratio in patients with acute heart failure: A cohort study Scientific Reports | (2019) 9:10639
17. Peng Yu,Ming Liu, Xue Yang, Ying Yu, Ji Zhao, Lei Zhang, Rui Tong, Hong Jiang, Yunzeng Zou, and Junbo Ge.Diagnostic Utility of ANG in Coronary Heart Disease Complicating Chronic Heart Failure: A Cross-Sectional Study.Hindawi Publishing Corporation Disease Markers Volume 2016, Article ID 2740826, 6 pages
18. Fontes JA, Rose NR, Cihakova D. The varying faces of IL-6: from cardiac protection to cardiac failure. Cytokine. 2015;74:62–68.
19. Volpe M, Rubattu S, Burnett J, Jr. Natriuretic peptides in cardiovascular diseases: current use and perspectives Eur Heart J. 2014;35:419–425.
20. Meijers WC, van der Velde AR, de Boer RA. Biomarkers in heart failure with preserved ejection fraction. Neth Heart J. 2016;24:252–258.
21. Gunnar Engstrom, MD, PhD; Olle Melander, MD, PhD; Bo Hedblad, MD, PhD Leukocyte Count and Incidence of Hospitalizations Due to Heart Failure Circ Heart Fail May 2009.
22. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, et al. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) developed withthe special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2016;37(27):2129–200.
23. Nicholas R. Jones1, Andrea K. Roalfe1, Ibiye Adoki2, F. D. Richard Hobbs1 and Clare J. Taylor1 Survival of patients with chronic heart failure in the community: a systematic review and meta-analysis protocol Systematic Reviews (2018) 7:151
24. Javed Butler Primary Prevention of Heart FailureISRN Cardiology Volume 2012, Article ID 982417, 15 pages
25. Jacqueline H Morris, Leway ChenExercise Training and Heart Failure: A Review of the Literature Cardiac Failure Review 2019;5(1):57–61.

TABLE-1&2
PROFORMA

SNO	Age	Gender	Diagnosis	CAUSE	Markers before treatment				Markers after treatment			
					CRP	CBP		ESR	CRP	CBP		ESR
						TLC	PLR			TLC	PLR	
1	62	M	HF	MI	24	11.5	151	12	0.16	10.5	88	8
2	78	F	HF	MI	0.78	11.4	110	6	0.43	9.8	108	2
3	55	M	HF	MI	12.98	9.6	130	2	0.43	8.7	126	3
4	56	M	HF	MI	1.0	10.7	102	8	4.0	9.8	147	14
7	77	M	HF	MI	13.87	11.1	128	7	0.76	11.7	148	2
6	68	F	HF	MI	0.166	8.7	142	1	0.87	10.8	150	1
7	47	F	HF	MI	22	10.1	110	4	0.87	8.5	149	1
8	66	M	HF	Cardiomyopathy	24.34	11.4	142	5	0.65	11.1	114	2
9	78	F	HF	MI	0.18	10.3	111	8	0.85	10.2	145	3
10	60	M	HF	HTN	3.14	9.7	158	7	0.87	10.1	123	8
11	43	F	HF	MI	24.2	11.8	110	20	0.36	11.2	72	14
12	55	F	HF	MI	0.87	10.1	132	1	0.68	8.2	168	6
13	78	F	HF	Valve disease	18.3	11.3	150	1	0.98	10.7	111	1
14	68	F	HF	MI	0.63	10.7	94	8	0.98	11.3	165	5
15	66	M	HF	MI,DM	17.23	8.7	101	10	0.76	9.7	111	2
16	40	F	HF	MI	21.5	12	85	9	0.86	9.2	142	1
17	67	F	HF	MI	3.14	8.6	121	23	0.89	12.1	107	28
18	65	M	HF	MI	23.3	8.9	103	12	0.76	11.1	156	3
19	60	F	HF	MI	0.17	12.2	107	1	0.90	10.4	115	8
20	55	M	HF	MI	0.76	10.9	110	8	0.90	9.2	142	9
21	43	M	HF	MI	0.68	11.7	113	11	0.49	12.2	125	6
22	59	M	HF	MI	29.6	11.2	144	2	0.76	8.9	130	3
23	55	M	HF	MI	25.6	8.9	157	1	0.88	9.7	166	1
24	78	M	HF	MI	22.6	10.2	89	1	0.43	10.2	170	1
25	70	M	HF	MI	23.9	10.4	109	6	0.65	10.4	109	2
26	43	M	HF	MI	33.2	11.6	107	5	0.87	9.2	159	4
27	56	F	HF	MI	24.1	10.8	138	11	0.35	9.1	94	4
28	76	M	HF	Cardiomyopathy	12.9	9.6	130	2	0.43	8.7	126	3
29	77	M	HF	ARRHYTHMIA	13.8	11.1	128	7	0.76	11.7	148	2
30	66	M	HF	HTN	3.14	9.7	158	87	0.87	10.1	122	8
31	43	F	HF	MYOCARDITIS	24.20	11.8	110	20	0.36	11.2	72	14
32	55	F	HF	MI	21.50	12.1	85	1	0.86	9.2	142	6
33	77	F	HF	MI	0.17	12.2	106	1	0.90	10.4	115	8
34	88	M	HF	MI	23.3	8.9	120	12	0.76	11.1	156	3
35	55	M	HF	HYPERTHYROIDISM	29.6	11.2	110	2	0.90	9.2	142	9
36	78	M	HF	HYPER THYROID	29.6	11.2	89	2	0.43	10.2	170	3
37	77	M	HF	DM	3.14	8.6	107	23	0.87	9.2	158	4
38	66	F	HF	CKD	24.1	10.8	138	11	0.35	9.1	94	4
39	65	M	HF	HYPER THYROID	23.3	8.9	103	12	0.76	11.1	156	3
40	55	M	HF	CKD	3.14	8.6	157	23	0.88	9.7	166	1
41	84	F	HF	SVT	21.51	12.1	85	9	0.86	9.2	142	1
42	71	F	HF	VALVE DI	18.34	11.3	150	1	0.98	10.7	111	1

				SEASE								
43	86	M	HF	HTN	3.14	9.7	158	87	0.87	10.1	122	8
44	43	M	HF	CKD	0.68	11.7	113	11	0.49	12.2	125	6
45	62	M	HF	HTN	24	10.5	150	3	0.16	10.7	88	2
46	78	F	HF	CKD	0.18	10.3	111	8	0.85	10.2	144	3
47	78	M	HF	PERICARDITIS	22.6	10.2	89	1	0.43	10.2	170	3
48	56	M	HF	SVT	0.75	10.7	102	8	4.48	9.8	147	14
49	43	F	HF	A.F	24.2	11.8	110	20	0.36	11.2	72	14
50	60	F	HF	HYPOTHYROID	0.17	12.2	107	1	0.90	10.4	115	8

Table 3: Paired T tes

iablesVar [N=50]	BEFORE Values TREATMENT		VALUES AFTER TREATMENT		p-value	SIGNIFICANCE
	MEAN	SD	MEAN	/SD		
CRP	13.99	11.15	1.68	6.0	0.00	‹0.05
TLC	12155	11030	12100	14163	0.91	›0.05
PLR	119	22.20	130	27.28	0.046	0.05‹
ESR	11.04	17.06	5.32	5.15	0.018	0.05‹

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