ORIGINAL ARTICLE

CORRELATION OF SERUM GALECTIN-3 LEVELS WITH EJECTION FRACTIONS IN HEALTHY SUBJECTS AND HEART FAILURE PATIENTS

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Background: High Galectin-3 levels are indicative of severity of heart diseases and are associated with increased risk of major adverse cardiovascular events including heart failure. The objective of this study was to determine correlation between ejection fraction and serum Galectin-3 levels recorded by simple and quick test. **Methods:** This cross-sectional analytical study was conducted at the Armed Forces Institute of Cardiology (AFIC) Rawalpindi. Thirty (30) healthy adults and 60 heart failure patients were selected through randomised sampling. Diagnosed cases were classified using modified NYHA classification. Group 1 included healthy adults, Group 2 included 30 mild heart failure subjects of NYHA class I and II, Group 3 included 30 severe heart failure subjects of NYHA class III and IV. Ejection fraction was recorded at AFIC with trans-thoracic echocardiography in supine and left lateral positions. Blood samples of the participants were used for estimation of Galectin-3 by ELISA using human serum Galectin-3 ELISA kit Catalogue No. E1951Hu (Bio Assay technology). Observations were recorded on proforma, Pearson's correlation test and ANOVA were performed using SPSS-24. **Results:** The LVEF was 70.7±2.78% in Group-1, 59.3±3.4% in Group-2, and 38.96±12.27% in Group-3. The LVEF showed a substantial negative correlation with serum Galectin-3 levels (r= -0.630, p<0.001). **Conclusion:** There is a significant negative correlation between Serum Galectin-3 and extent of functional changes of left ventricle recorded by Ejection fraction on echocardiography.

Keywords: Heart Failure, Galectin-3, Echocardiographic parameters, Ejection fraction

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INTRODUCTION

Heart failure (HF) is a terminal cardiac disease and carries risk of morbidity and mortality. It has multiple aetiologies and many of the cardiovascular diseases and coronary artery diseases end up in heart failure. Heart failure can be categorized by cardiac remodelling; ventricular dysfunction and fibrosis.[1] Several biomarkers have been established for diagnosis and prognosis of heart failure. One novel blood marker approved by Food and Drug Administration for its role in fibrosis is Galectin-3. Various recent clinical studies show that Galectin-3 mediates fibrosis in a variety of organ systems including heart, thus it is considered as a biomarker that reflects ventricular remodelling.[2] In Pakistani population, however, no such studies have been carried out and such correlation has not been determined.

Galectin-3 belongs to multifunctional lectin family.[3] It is a protein that serves to bind Galactoside, thus helping in cell-to-cell adhesion and cell matrix interactions. Galectin-3 causes myofibroblast proliferation, fibrogenesis and inflammation.[4] Echocardiographic parameters give us an idea of heart functioning, structure, remodelling and severity of heart disease.[5] Cardiac pathologies bringing about a change in functioning of heart result in altered ejection fraction and can be assessed by echocardiographic measurement.

In recent times of pandemic outbreak where emergency patients were not immediately put on echocardiography machine until the COVID-19 results were available, there was a need for a simple and affordable test that could provide the assessment of ventricular remodelling and functioning. Serum Galectin-3 levels could prove to be the missing indicator. This study aimed to provide a biomarker assessment in heart failure patients for determining the extent of ventricular remodelling and associated ejection fraction changes. This study can fill in the existing knowledge gap regarding South-Asian population in general and Pakistani population in particular.

METHODOLOGY

This study was conducted at Army Medical College and Armed Forces institute of Cardiology (AFIC), Rawalpindi after the formal approval from ethics review boards. The Heart failure patients admitted or visiting outpatient department (OPD) from July 2020 to October 2020 were selected. Sampling technique was Non probability purposive and WHO calculator of sample size was employed for calculating sample size. Heart failure patients were diagnosed on the basis of Framingham's criteria and classified using New York Heart Association (NYHA) classification into class I–IV depending upon severity. For our study we took ninety

adults (age range 19–65 years) and divided them into three groups using modified NYHA classification. Group 1 included healthy adults. Group 2 included 30 mild heart failure patients in NYHA class I and II whereas Group 3 included 30 severe heart failure patients in NYHA class III and IV.

Participants were assessed for the fulfilment of inclusion criteria and those having endocrine abnormalities, inflammatory disorders, cancers and using anti-inflammatory drugs were excluded from the study. All participants provided a written informed consent. Their demography and history were recorded and physical examination was carried out. Levels of Galectin-3 were recorded from blood serums of all the participants by ELISA.

The procedures followed were consistent with the ethical standards of Armed Forces Institute of Cardiology ethics review board. The research was designed in accordance with the Helsinki Declaration 1975, as revised in 1983.

We took measurements of 90 participants divided into three groups based on severity of Heart Failure using the modified NYHA classification. Ejection fraction was recorded and calculated on Trans-thoracic echocardiography. Means of Ejection fraction for each group were also recorded.

Serum Galectin-3 levels were recorded from the blood samples of all participants using Enzyme linked Immunosorbent Assay human serum Galectin-3 kit.[6] The study variables Left ventricular Ejection Fraction (LVEF) and serum Galectin-3 levels are quantitative hence these were correlated using Pearson's correlation. The data was analysed using SPSS-24. The ejection fraction and Galectin 3 were recorded in the three study groups.

RESULTS

With worsening heart failure, serum Galectin-3 levels increased indicating underlying processes of myocardial remodelling and fibrosis. The mean ejection fraction of the group 1 (healthy adults) was found to be 70.7±2.78%, for group 2 (mild heart failure NYHA I and II)) it was 59.3±3.4% and that of group 3 (severe heart failure NYHA III and IV) it was 38.96±12.27% as shown in Table-1. There is a significant negative correlation between ejection fraction and serum Galectin-3 levels (r= -0.630, p<0.001) (Figure-1).

Table-1: Ejection fraction in healthy adults, mild heart failure patients and severe heart failure patients (Mean±SD)

Echocardiographic Parameter	Group-1 Healthy adults	Group-2 NYHA (I & II)	Group-3 NYHA (III & IV)	*p*
LVEF (%)	70.7±2.78	59.3±3.4	38.96±12.27	<0.001*

*Significant

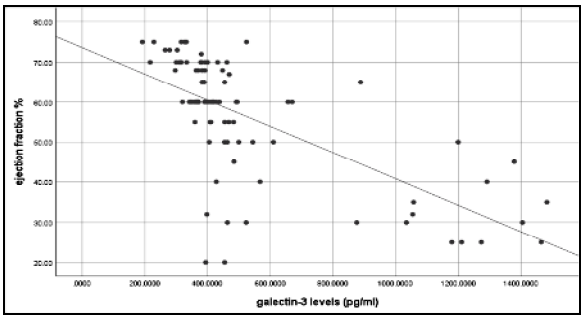

Figure-1: Correlation of serum Galectin-3 and LVEF

DISCUSSION

We associated left ventricular ejection fraction changes to levels of a biomarker which could be recorded by a quick blood test. These levels could help during the initial management and risk stratification of the heart failure patients especially in pandemic conditions where other investigations were difficult and restricted.

In this study left ventricular ejection fraction was recorded in all 90 subjects and Pearson's correlation analysis was used to find correlations between the recorded Ventricular ejection fractions and the Galectin-3 levels. With progressive decrease in ejection fraction, greater Galectin-3 levels were seen depicted by significant and negative *r* values.

Recent studies have evaluated the relationship between ejection fraction and Galectin-3 levels systematically. The Deventer-Alkmaar Heart Failure Clinic Project: DEAL-HF trial conducted echocardiographic evaluation of 240 heart failure patients and found a negative association between serum Galectin-3 and LVEF.[7] In a study on 100 patients with LV dysfunction Pearson correlation analysis was conducted to correlate the levels of serum Galectin-3 with echocardiographic indices of HF patients. The levels of serum Galectin-3 had highly significant negative correlation with LV ejection fraction.[8] In a study including 63 cases of heart failure with ejection fraction ≥50%, confirmed with echocardiography, Galectin-3 levels in serum were measured using an enzyme-linked-immunosorbent serologic assay. The values were significantly higher in heart failure cases compared with the control group.[9] Yin *et al*[10] found the mean Galectin-3 levels significantly higher in HFpEF patients versus healthy controls (23.09 *vs* 16.74 ng/mL, p<0.0001). Another study showed similarity in results when Pearson correlation analysis was conducted to correlate the levels of serum Galectin-3 with echocardiographic indices of HF patients. Galectin-3 levels had highly significant negative correlation with LVEF (p<0.001).[11] A Research conducted on 115 patients of heart failure revealed a negative correlation between the LVEF and Galectin 3 levels (r= -0.139).[12] Our findings are in agreement and coherent with these observations.

There have been contradicting studies as well. In a study on Chinese population including 133 chronic HF patients and 45 decompensated HF patients no association between myocardial function (indicated by echocardiographic reading such as LVEF) and plasma concentrations of serum Galectin-3 was found.[13] There is strong evidence of reduced efficiency of Galectin-3 as a bio-marker in various ethnicities. In a sub-study of the Atherosclerosis Risk in Communities observational cohort including 1,375 white patients and 434 black patients, Galectin-3 was found to be associated with heart failure and mortality among white patients and not among black patients.[14]

No such studies have been conducted on Pakistani population until now providing a room for further study to fill the knowledge gap. Our study was a cross-sectional study and the levels of biomarkers were measured at a single time; it is therefore possible that the longitudinal trajectory of change in biomarkers may provide additional causal inferences.

CONCLUSION

Galectin-3 levels are associated with abnormalities of myocardial function related to heart failure. Serum Galectin-3 is a diagnostic biochemical marker for heart failure and indicates severity of disease quantitatively. Serum Galectin-3 level is closely correlated to the degree of left ventricular structural and functional changes observed on echocardiography in heart failure.

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REFERENCES

1. Oppedisano F, Mollace R, Tavernese A, Gliozzi M, Musolino V, Macrì R, *et al.* PUFA supplementation and heart failure: effects on fibrosis and cardiac remodeling. Nutrients 2021;13(9):2965.
2. Amin HZ, Amin LZ, Wijaya IP. Galectin-3: a novel biomarker for the prognosis of heart failure. Clujul Med 2017;90(2):129–32.
3. Romero A, Gabius HJ. Galectin-3: is this member of a large family of multifunctional lectins (already) a therapeutic target? Expert Opin Ther Targets 2019;23(10):819–28.
4. Barman SA, Li X, Haigh S, Kondrikov D, Mahboubi K, Bordan Z, *et al.* Galectin-3 is expressed in vascular smooth muscle cells and promotes pulmonary hypertension through changes in proliferation, apoptosis, and fibrosis. Am J Physiol Lung Cell Mol Physiol 2019;316(5):L784–97.
5. Špinarová M, Meluzin J, Podroužková H, Štěpánová R, Špinarová L. New echocardiographic parameters in the diagnosis of heart failure with preserved ejection fraction. Int J Cardiovasc Imaging 2018;34(2):229–35.
6. Devereux RB, de Simone G, Arnett DK, Best LG, Boerwinkle E, Howard BV, *et al.* Normal limits in relation to age, body size and gender of two-dimensional echocardiographic aortic root dimensions in persons ≥15 years of age. Am J Cardiol 2012;110(8):1189–94.
7. Pulignano G, Del Sindaco D, Jaarsma T, Stromberg A, Martensson A, Dracup K, *et al.* 264 Translation and validation of the Italian version of the European heart failure self-care behaviour scale. Eur J Heart Fail Suppl 2004;3(1):64.
8. Mosleh W, Chaudhari MR, Sonkawade S, Mahajan S, Khalil C, Frodey K, *et al.* The therapeutic potential of blocking galectin-3 expression in acute myocardial infarction and mitigating inflammation of infarct region: a clinical outcome-based translational study. Biomark Insights 2018;13:1–10. DOI: 10.1177.1177271918771969.
9. Kanukurti J, Mohammed N, Sreedevi N, Khan SA, Baba KS, Bhaskar MV, *et al.* Evaluation of galectin-3 as a novel diagnostic biomarker in patients with heart failure with preserved ejection fraction. J Lab Physicians 2020;12(2):126–32.
10. Yin QS, Shi B, Dong L, Bi L. Comparative study of galectin-3 and B-type natriuretic peptide as biomarkers for the diagnosis of heart failure. J Geriatr Cardiol 2014;11(1):79–82.
11. Fernando ML, Krithika B, Silambanan S. Galectin-3: A novel biomarker of left ventricular remodelling in chronic heart failure. J. Evid. Based Med. Healthc 2020;7(16):816–22.
12. Shah RV, Chen-Tournoux AA, Picard MH, van Kimmenade RR, Januzzi JL. Galectin-3, cardiac structure and function, and long-term mortality in patients with acutely decompensated heart failure. Eur J Heart Fail 2010;12(8):826–32.
13. Tang WH, Shrestha K, Shao Z, Borowski AG, Troughton RW, Thomas JD, *et al.* Usefulness of plasma galectin-3 levels in systolic heart failure to predict renal insufficiency and survival. Am J Cardiol 2011;108(3):385–90.
14. McEvoy JW, Chen Y, Halushka MK, Christenson E, Ballantyne CM, Blumenthal RS, *et al.* Galectin-3 and risk of heart failure and death in blacks and whites. J Am Heart Assoc 2016;5(5):e003079.

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