ORIGINAL ARTICLE

Relationship of Biochemical Parameters and Echocardiogram Findings with Appetite in Patients having Reduced Ejection Fraction Heart Failure

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ABSTRACT

Objective: To determine the relationship of biochemical parameters and echocardiogram findings with appetite and nutritional status in patients with heart failure with reduced ejection fraction.

Study Design: Cross-sectional study.

Place and Duration of Study: This study was conducted at the Department of Medicine, Combined Military Hospital (CMH), Peshawar, Pakistan, from February 2022 to August 2022.

Methods: The study was conducted on adult patients with heart failure for at least three months. Indoor patients, those with hospitalization within the last four weeks, and unwilling patients were excluded. The Council on Nutrition Appetite Questionnaire and Mini Nutritional Assessment questionnaire were administered in direct face-to-face interviews. A transthoracic echocardiogram was done to document the left ventricular ejection fraction. Different hematological and biochemical parameters were also analyzed.

Results: There were 76 patients aged 55.92± 15.22 years. Mean mini nutritional assessment and Council on Nutrition appetite questionnaire scores were 17.89± 5.23 and 20.74± 8.19, respectively. Based on mini nutritional assessment scores, 36 were malnourished, 27 were at risk of malnutrition, and 13 had normal nutritional status. Using Council on Nutrition appetite questionnaire scores, 57 were at risk of malnutrition, while 19 had no risk. Left ventricular ejection fraction and hemoglobin were lower in malnourished patients. However, there were no differences in other biochemical parameters amongst patients with good or poor nutritional status.

Conclusion: Patients with heart failure had poor appetite and nutritional status proportionate to the degree of left ventricular systolic dysfunction.

Keywords: *Anorexia, Ejection Fraction, Heart Failure, Malnutrition.*

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Introduction

Cardiovascular diseases are a leading cause of mortality worldwide, making up 32.2% of all deaths as per data released by World Health Organization in Global Health Estimates 2019.[1] Although south-Asian countries, including Pakistan, account for one fourth of world population, more than half of global burden of heart diseases is borne by these nations.[2] There were at least 2.8 million cases of heart failure (HF) in Pakistan in 2006.[3] The Latest local epidemiological data on this subject is not available. However, it is not unfair to conclude that this number would have increased exponentially by now because of the sharp rise in the incidence of diabetes and coronary heart disease. This increasing trend was also documented in a study from Peshawar almost previously.[4]

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Complications of HF can involve the central nervous system in the form of stroke and vascular dementia, kidneys in the form of renal failure, the liver in the form of congestive hepatopathy, the lungs in form of pulmonary hypertension or pulmonary edema and the gastrointestinal system as intestinal edema and ascites.[5] HF may lead to malabsorption by redirecting blood flow from the gastrointestinal system to other vital organs. Due to low blood flow and impaired venous return (due to HF), intestinal permeability may, in turn, increase, causing translocation of pathogens across the gut. This leads to a continuous inflammatory state and raised inflammatory markers in HF.[6] A low blood flow across the gastrointestinal tract and inflammatory state combined with renal and hepatic complications lead to anorexia, which is further complicated by malabsorption due to intestinal edema and recurrent gastrointestinal infections due to altered permeability, resulting in cardiac cachexia.[7] As HF worsens, so do its systemic complications, and thus, it can be hypothesized that it will lead to worsening of nutritional status, anorexia, cardiac cachexia, and vice versa. Appetite and nutritional status in these individuals can be assessed using the Council of Nutrition Appetite Questionnaire (CNAQ) and the Mini Nutritional Assessment (MNA) score.

We carried out this study to determine the relationship of biochemical parameters and echocardiogram findings with appetite in patients with reduced ejection fraction heart failure. The results would help identify the magnitude of the problem and then implement strategies to identify such patients and initiate steps to improve their nutritional status.

Methods

This cross-sectional study was conducted at the Department of Medicine, Combined Military Hospital (CMH), Peshawar, Pakistan, from February 2022 to August 2022. The Ethics Review Committee for Medical and Biomedical Research of Combined Military Hospital (CMH), Peshawar, Pakistan, approved the study design and issued the ethical review certificate via serial number 51 on 13th August 2021, before the start of data collection. All the participants provided written consent beforehand. Sample size calculation was performed with ANOVA: Fixed effects, omnibus, one-way test using G*Power software version 3.1.9.7. Power was set at 0.8 and significance level at 0.05 for this test. A minimum of 57 patients were required, assuming ejection fractions of 30%, 32%, and 31.5% amongst malnourished patients, those at risk of malnutrition, and those with normal nutritional status, respectively, as described by Özyiğit et al.[7]

Using convenience sampling, we included outdoor patients.

Inclusion criteria: Adults aged 18-60 years, patients on treatment for heart failure for at least three months, who had stable cardiac function based on clinical assessment.

Exclusion criteria: Unwell hospital patients, those with a history of hospitalization within the last four weeks, and unwilling patients were excluded.

Demographic data were collected for all eligible patients visiting the Outpatient Department for the first time during the study period. Nutritional assessment was done in two ways. The Council on Nutrition Appetite and Mini Nutritional Assessment questionnaires were then administered in direct face-to-face interviews. All patients had a transthoracic echocardiogram done the same day to document left ventricular ejection fraction (LVEF). Finally, blood samples were collected for estimation of different hematological and biochemical parameters, including hemoglobin, serum sodium, potassium, albumin, pro-BNP, calcium, random plasma glucose, cholesterol, triglycerides, ferritin, urea, creatinine, and alanine transaminase. All the blood samples were analyzed in the Pathology Laboratory of this hospital, except Pro-BNP levels, for which serum samples were sent to the Armed Forces Institute of Pathology (AFIP), Rawalpindi.

Data were s analyzed using Social Package for Statistical Sciences (SPSS) version 24. All variables with parametric distribution were described as mean± standard deviation, whereas those with non-parametric distribution i.e. Pro-BNP and Ferritin were presented as median and interquartile range. MNA and CNAQ scores were categorized into different classes as per the standard recommendations. One-way ANOVA test was used to compare values of different echocardiographic and biochemical variables in the three categories of

MNA scores. CNAQ scores were categorized into different classes as per the standard recommendations. There were two categories, so the variables with normal distribution were compared using the Independent Samples t-Test, whereas those with non-parametric distribution were compared using the Independent Samples Mann-Whitney U-Test. The level of significance was set at 5% for all comparisons.

Results

In this study, there were 76 patients aged 55.92± 15.22 years. Baseline characteristics are shown in Table-1. Mean MNA and CNAQ scores were 17.89± 5.23 and 20.74± 8.19 respectively. Based on MNA scores, 36 were malnourished, 27 were at risk of malnutrition and 13 had normal nutritional status. Using CNAQ scores, 57 were at risk of malnutrition, while 19 had no risk.

Post-hoc analysis revealed a much higher LVEF amongst patients with normal nutritional status (p=0.001 for comparison with at risk group, and p<0.001 for comparison with malnourished group), while the differences amongst malnourished and at-risk patients were insignificant (p=0.143). Hemoglobin levels were significantly lower amongst malnourished patients as compared to those with normal nutritional status (p=0.037), whereas the differences amongst the other categories were insignificant.

As shown in Table-2, left ventricle ejection fraction and hemoglobin levels were significantly different amongst patients in different categories of MNA scores, whereas differences in other biochemical parameters were insignificant.

Table - 1: Baseline characteristics

Parameter		Value
Age (years) mean ± SD		55.92± 15.22
Gender n (%)	Male	57(75.00%)
	Female	19(25.00%)
Duration of heart failure mean ± SD		6.91± 2.20
New York Heart Association (NYHA) class n (%)	I	6(7.89%)
	II	26(34.21%)
	III	31(40.79%)
	IV	13(17.11%)
Co-morbidities n (%)	Diabetes mellitus	37(48.68%)
	Hypertension	40(52.63%)
	Peripheral vascular disease	6(7.89%)
	Stroke	11(14.47%)
	Pulmonary hypertension	22(28.95%)
	Chronic kidney disease	55(72.37%
Mean MNA score ± SD		17.89± 5.23
Mean CNAQ score ± SD		20.74± 8.19

Left ventricle ejection fraction was significantly lower amongst patients at a higher risk of malnutrition based on CNAQ scores. However, there were no differences in various biochemical parameters amongst the two groups, as reflected in Table-3.

Discussion

This study has provided alarming results. Only one in every four to five patients with heart failure had a normal nutritional status and was not at risk of developing malnutrition. This was related to the ejection fraction, and there was a direct linear relationship of nutritional status with hemoglobin levels.

In our study, 82.9% of participants had impaired nutritional status, i.e., they were either malnourished (47.4%) or were at risk of malnutrition

Table - 2: Echocardiographic and biochemical parameters compared among different categories of Mini Nutritional Assessment (MNA) scores

Parameter	MNA Score			*P*-Value
Score Category	**<17 (Malnourished)**	**17 - 23.5 (At risk)**	**≥24 (Normal)**	
LVEF (%)	34.06± 10.52	38.74± 8.12	49.00± 7.10	<0.001
Hb (g/dL)	9.01± 1.16	9.38± 1.61	10.08± 0.97	0.047
Serum sodium (mmol/L)	131.78± 5.24	130.52± 4.36	133.85± 10.63	0.292
Serum potassium (mmol/L)	4.47± 0.73	4.65± 0.65	4.76± 0.58	0.352
Albumin (g/L)	34.22± 5.97	34.96± 6.17	36.31± 5.31	0.553
Serum calcium (mmol/L)	1.68± 0.55	1.86± 0.50	1.64± 0.59	0.351
Random plasma glucose (mg/dL)	196.42± 38.82	194.78± 41.69	172.46± 32.17	0.151
Cholesterol (mmol/L)	3.60± 1.31	3.22± 1.14	3.62± 1.16	0.427
Triglycerides (mmol/L)	2.76± 0.84	3.26± 1.11	3.05± 1.39	0.176
Serum urea (mmol/L)	10.78± 4.86	12.08± 4.85	10.16± 3.74	0.399
Creatinine (µmol/L)	163.33± 73.80	240.07± 216.35	177.85± 68.97	0.102
Alanine aminotransferase (U/L)	23.56± 9.12 208	28.67± 9.66	25.69± 10.77	0.120
*Ferritin (ng/ml)	208 (150.50-276)	191(157 -271)	242(162-653)	0.658
Pro-BNP (pg/ml)	2187(104.50 7137.50)	3397(845 -11331)	953(850.50 - 3110)	0.213

**Pro-BNP and Ferritin were having skewed distribution. Therefore, we have used median and interquartile ranges for these parameters*

(35.5%) using MNA score. This number is significantly higher than quoted in similar studies. Kaluzna-Oleksy et al. reported a prevalence of 55% impaired nutritional status using MNA scale.[8] Similarly, Bonilla-Palomas et al. reported a malnutrition prevalence of 72.6%. However, their study was primarily based on hospitalized patients.[9] Using CNAQ score, 75% individuals in our study were found to have poor appetite. This number is also significantly higher than that reported by corresponding studies. As an example, amongst patients with stable heart function, Andreae et al. reported an incidence of poor appetite with a risk of future weight loss at 38%.[10] A higher prevalence of malnutrition amongst our patients could be due to differences in socio-economic status. In a study done in 2015 by Ahmed et al., 51.3% of elderly people from Pakistan had poor nutritional status.[11]

We observed a direct link between nutritional status/ appetite and ejection fraction. This result contrasts with previous studies where a direct link between left ventricular function and nutritional status or appetite was not found. Kaluzna-Oleksy et al. demonstrated a non-significant difference among patients with normal nutritional status who were at risk of malnutrition or malnourishment. However, they only included patients with LVEF <40%.[8] Similarly, Al-Najjar et al. did not see a significant

Table-3: Echocardiographic and biochemical parameters compared amongst Council of Nutrition Appetite Questionnaire (CNAQ) Score

Parameter	CNAQ score		*P*-Value
	<28 (At risk)	>28 (No Risk)	
LVEF (%)	34.33±8.47	50.11±6.54	<0.001
Hb (g/dL)	9.27±1.37	9.50±1.30	0.517
Serum sodium (mmol/L)	131.70± 5.82	131.63± 7.66	0.971
Serum potassium (mmol/L)	4.55±0.71	4.70±0.59	0.424
Albumin (g/L)	34.58±6.29	35.63±4.65	0.441
Serum urea (mmol/L)	11.13±4.55	11.14±5.19	0.994
Serum calcium (mmol/L)	1.76±0.52	1.66±0.61	0.540
Random plasma glucose (mg/dL)	194.04± 37.56	184.84± 44.73	0.427
Cholesterol (mmol/L)	3.45±1.30	3.51±0.99	0.877
Triglycerides (mmol/L)	2.97±0.99	3.06±1.26	0.759
Creatinine (µmol/L)	177.95± 81.83	238.47± 250.78	0.114
Alanine transaminase (U/L)	24.96± 9.32	28.05± 10.90	0.278
*Pro-BNP (pg/ml)	2387(1005-8188.50)	953(867-3276)	0.107
Ferritin(ng/ml)	228(167-299.50)	165(145-567)	0.464

**Pro-BNP and Ferritin were having skewed distribution. Therefore, we have used median and interquartile ranges for these parameters*

difference in left ventricular dysfunction using the nutritional risk index between HF patients at risk and those not at risk of malnutrition.[12]

The only parameter difference between patients with good or poor nutritional status assessed by MNA score was hemoglobin. However, this was not the case when evaluated using CNAQ. A deficiency of micronutrients can explain the relationship of anemia with a degree of malnutrition due to mal-absorption and systemic inflammation causing raised hepcidin.[13,14] Anemia further complicates HF by reducing peripheral oxygen supply, resulting in increased workload on already failing heart and worsening dyspnea class. In some studies, an inverse link between ejection fraction and hemoglobin has been seen, i.e., lower ejection fraction leading to polycythemia.[15] This is postulated to be secondary to decreased perfusion of kidneys, which results in higher levels of erythropoietin, leading to erythropoiesis. But for this mechanism to work, the patient should be adequately nourished, such that building blocks required for hemoglobin and red blood cell production are readily available.

Other laboratory parameters such as serum Pro-BNP, electrolytes, creatinine, urea, alanine transaminase, albumin, bilirubin, or CRP measured in our study did not show any significant difference amongst individuals with subgroups defined by MNA score or CNAQ score. This result is in accordance with those seen in the study by Kaluzna-Oleksy et al. where NT-proBNP levels did not correlate with MNA subgroups either.[8] However, in our study, a significant difference can be seen if we compare pro- BNP levels of malnourished individuals and those at risk of malnutrition separately with individuals not at risk of malnutrition. Sze et al. studied the prognostic value of malnutrition in patients with HF.[16] They found higher pro-BNP levels in malnourished individuals.

Malnutrition is one of the most common complications of HF. Due to lack of randomized controlled trials on nutritional issues, evidence-based medicine sometimes tends to bias physicians

against the power of dietary approaches in managing certain diseases.[17] In HF, a multitude of factors affecting the gastrointestinal, hepatic, renal, and cardiovascular systems play together in a way that reduces appetite, causes mal-absorption, reduces circulation, increases systemic inflammatory response, and causes protein and fat catabolism resulting in a malnourished state.[18]

In this study, we have used two different questionnaires for the assessment of appetite and nutritional status. The CNAQ consists of eight validated questions. It was derived from The Appetite, Hunger, and Sensory Perception Questionnaire, which consisted of 29 questions in October 1999 using the Delphi technique. It was later validated in multiple studies on elderly nursing home residents as well as patients with cancer or heart disease.[19] Mini Nutritional Assessment was developed in early 1990s, consisting of 18 assessment markers which ranged from simple questions to specific general and psychological examinations. It was initially developed by Nestle Nutrition to screen malnutrition in the elderly. Its validity has been shown in various publications regarding quality of life, morbidity, and mortality in many disorders.[20,21] Malnutrition is said to be an independent marker of mortality in HF. As our research was cross-sectional, we cannot comment on mortality and morbidity related to low appetite or malnutrition. However, MNA and MNA short forms have been assessed and validated to be good predictors of mortality in patients with HF.[22] Similarly, improving nutritional status in these patients is an important therapeutic step to improve prognosis in these cases.

This research had several limitations, and the results should be interpreted in this context. It is a single-center cross-sectional study so it might be difficult to generalize the results to other setups or determine a cause-effect relationship. The patients were enrolled in outdoor clinics and had stable heart failure. We also did not segregate patients with reduced or preserved heart failure.

Conclusion

Nutrition remains an ignored subject in the management of heart diseases. This study highlights the positive correlation of left ventricular function with objective scores for appetite and malnutrition. Therefore, it is stressed that consideration of a patient's nutritional status must be included during the assessment, and appropriate management must be advised.

REFERENCES

1. Anonymous. Global Health Estimates. n.d. Available from: https://www.who.int/data/global- health-estimates [Last accessed: 3/2/2023].
2. Martinez-Amezcua P, Haque W, Khera R, Kanaya AM, Sattar N, Lam CS, et al. The upcoming epidemic of heart failure in South Asia. Circulation: Heart Failure. 2020; 13: e007218. doi: 10.1161/CIRCHEARTFAILURE.120.007218.
3. Sheikh SA. Heart failure in Pakistan: A Demographic Survey. Journal of Cardiac Failure. 2006; 12: S157. doi: 10.1016/j.cardfail.2006.08.069.
4. Noor L, Adnan Y, Khan SB, Shah SS, Sawar S, Qadoos A, et al. Inpatient burden of heart failure in the cardiology units of tertiary care hospitals in Peshawar. Pakistan Journal of Physiology. 2012; 8: 3-6.
5. Murphy SP, Kakkar R, McCarthy CP, Januzzi Jr JL. Inflammation in heart failure: JACC state-of-the-art review. Journal of the American College of Cardiology. 2020; 75: 1324-40. doi: 10.1016/j.jacc.2020.01.014.
6. Soto ME, Pérez-Torres I, Rubio-Ruiz ME, Manzano-Pech L, Guarner-Lans V. Interconnection between cardiac cachexia and heart failure—Protective role of cardiac obesity. Cells. 2022; 11: 1039. doi: 10.3390/cells11061039.
7. Özyiğit İİ, Koçyiğit B, Söyleyici B, Uçar FM. Evaluation of malnutrition statuses in systolic heart failure patients. Turkish Medical Student Journal. 2019; 6. doi: 10.4274/tmsj.galenos.2019.06.01.03.
8. Kaluzna-Oleksy M, Sawczak F, Kukfisz A, Szczechla M, Krysztofiak H, Wleklik M, et al. Appetite and nutritional status as potential management targets in patients with heart failure with reduced ejection fraction—The relationship between echocardiographic and biochemical parameters and appetite. Journal of Personalized Medicine. 2021; 11: 639. doi: 10.3390/jpm11070639.
9. Bonilla-Palomas JL, Gámez-López AL, Moreno-Conde M, López-Ibáñez MC, Castellano-García P, Ráez-Ruiz CJ, et al. Influencia de la desnutrición sobre la mortalidad a largo plazo en pacientes ambulatorios con insuficiencia cardiaca crónica. Nutrición Hospitalaria. 2017; 34: 1382-9. doi: 10.20960/nh.1131.
10. Andreae C, Strömberg A, Årestedt K. Prevalence and

associated factors for decreased appetite among patients with stable heart failure. Journal of Clinical Nursing. 2016; 25: 1703-12. doi: 10.1111/jocn.13220.

11. Ahmad AMR, Ronis KA. Nutritional status of Pakistan's elderly population: a comparative review with low to middle income countries. Pak Journal of Public Health. 2015; 5: 22–5.
12. Al-Najjar Y, Clark AL. Predicting outcome in patients with left ventricular systolic chronic heart failure using a nutritional risk index. The American journal of cardiology. 2012; 109: 1315-20. doi: 10.1016/j.amjcard.2011.12.026.
13. Anand IS, Gupta P. Anemia and Iron Deficiency in Heart Failure: Current Concepts and Emerging Therapies. Circulation. 2018; 138: 80–98. doi: 10.1161/ CIRCULATIONAHA.118.030099.
14. Gadayev AG, Turakulov RI, Kurbonov AK, Rakhimova ME. Role of Hepcidin and Pro-Inflammatory Cytokines in Chronic Heart Failure in Combination with Anemia. Central Asian Journal of Medicine. 2019; 3: 81-92.
15. Hsieh CC, Kuo FH, Liao CT. Heart Failure and Polycythemia: A Case Report and Literature Review. Acta Cardiological Sinica. 2022; 38: 532–5. doi: 10.6515/ACS.202207_38(4). 20220221C.
16. Sze S, Pellicori P, Kazmi S, Rigby A, Cleland JG, Wong K, et al. Prevalence and prognostic significance of malnutrition using 3 scoring systems among outpatients with heart failure: a comparison with body mass index. JACC: Heart Failure. 2018; 6: 476-86. doi: 10.1016/j.jchf.2018.02.018.
17. Kaegi-Braun N, Baumgartner A, Gomes F, Stanga Z, Deutz NE, Schuetz P. Evidence-based medical nutrition–A difficult journey, but worth the effort. Clinical nutrition. 2020; 39: 3014-8. doi: 10.1016/j.clnu.2020.01.023.
18. Ishikawa Y, Sattler ELP. Nutrition as Treatment Modality in Heart Failure. Current Atherosclerosis Reports. 2021; 23: 1-9. doi: 10.1007/s11883-021-00908-5.
19. Wilson MM, Thomas DR, Rubenstein LZ, Chibnall JT, Anderson S, Baxi A, et al. Appetite assessment: simple appetite questionnaire predicts weight loss in community-dwelling adults and nursing home residents. The American journal of clinical nutrition. 2005; 82: 1074-81. doi: 10.1093/ajcn/82.5.1074.
20. Soysal P, Isik AT, Arik F, Kalan U, Eyvaz A, Veronese N. Validity of the mini-nutritional assessment scale for evaluating frailty status in older adults. Journal of the American Medical Directors Association. 2019; 20: 183-7. doi: 10.1016/j.jamda.2018.07.016.
21. Krishnamoorthy Y, Vijayageetha M, Saya GK. Validation and Reliability Assessment of the Mini- Nutritional Assessment–Short Form Questionnaire among Older Adults in South India. Indian Journal of Community Medicine: Official Publication of Indian Association of Preventive & Social Medicine. 2021; 46: 70-4. doi: 10.4103/ijcm.IJCM_208_20.
22. Joaquín C, Alonso N, Lupón J, de Antonio M, Domingo M, Moliner P, et al. Mini Nutritional Assessment Short Form is a morbi-mortality predictor in outpatients with heart failure and mid-range left ventricular ejection fraction. Clinical Nutrition. 2020; 39: 3395-401. doi: 10.1016/j.clnu. 2020. 02.031.

Authors Contribution

BS: Idea conception, study designing, data collection, data analysis, results and interpretation, manuscript writing, and proof reading

ARA: Idea conception, study designing, data collection, data analysis, results and interpretation, manuscript writing, and proof reading

MH: Idea conception, study designing, data collection, data analysis, results and interpretation, manuscript writing, and proof reading