The association between lymphocyte count in cases of chronic heart failure

Submitted to department of medicine

College of medicine /Al-Nahrain university as

Apart of M.B.Ch.B graduation requirement

Edited By : Mustafa Mohammed Abd Al sahib

SUPERVISOR : prof. Waseem F Al-Tameemi

2018 – 2019

بسم الله الرحمن الرحيم

(يرفع الله الذين امنو منكم والذين اوتوا العلم درجات والله بما تعلمون خبير)

صدق الله العظيم

سورة المجادلة الأية رقم 11

Acknowledgement :

I would like to express my gratitude for my supervisor Dr. waseem F Al-tameemi for his support and direction, and to everyone who show me support.

Dedication :

To my family, my friend, and to all people who had help me to do this research.

Content :

List of table

List of figure

Abstract

Back ground :

Heart failure is the state that develops when the heart cannot maintain an adequate cardiac output. The lymphocyte are derived from pluripotent hematopoietic stem cells in the bone marrow there are two type (T and B) cell.

Aim : to define any lymphocyte count abnormalities in patient with chronic heart failure and its relation to clinical presentation.

Patient and method : Cross sectional study was performed during a period between October 2018 to January 2019 at Al-Imamian Alkadymian medical city, Baghdad, Iraq. Included randomly selected 30 participants who were diagnosed to have chronic HF based on symptoms and echocardiography, all the patient underwent clinical evaluation as well as CBC (WBC, lymphocyte count), and echo parameter EF %.

Result : female is predominant 18 cases (60%), the mean age is 64.8± 11.29 yr, the largest group with stage III,IV, the systolic HF is involved in 21 patient, the mean of echo-EF is 47%± 12.78, the mean of lymphocyte count is 1.51± 0.99, and the percentage is 17.45%± 15.88, the lymphocytopenia is involved in 19 patient 63.3%.

Conclusion :

* low lymphocyte count is a recognized feature in patient with chronic heart failure.

* male patient showed lower lymphocyte count than female.

1- Introduction

1.1- Heart failure:

Heart failure is an imprecise term used to describe the state that develops when the heart cannot maintain an adequate cardiac output or can do so only at the expense of an elevated filling pressure in mildest forms of heart failure, cardiac output is adequate at rest and becomes inadequate only when the metabolic demand increase during exercise or some other form of stress.[1,2]

1.1.1-etiology and pathophysiology :

1- reduced ventricular contractility: myocardial infarction , myocarditis ,cardiomyopathy .

2- ventricular outflow obstruction (pressure overload): hypertension, aortic stenosis(left heart failure), pulmonary hypertension, pulmonary valve stenosis(right heart failure) .

3- ventricular inflow obstruction : mitral stenosis, tricuspid stenosis .

4- ventricular volume overload : LV volume overload (e.g. mitral or aortic regurgitation, arteriovenous fistula), ventricular septal defect, RV volume overload (e.g. atrial septal defect), increased metabolic demand (high output)

5- arrhythmia: atrial fibrillation , tachycardia cardiomyopathy , complete heart block .

6- diastolic dysfunction (diastolic heart failure or called heart failure with preserved EF): coronary artery disease, LVH and

fibrosis secondary to chronic HTN or severe AVS, constrictive pericarditis, cardiac tamponed, restrictive cardiomyopathy. [1]

1.1.2- precipitating factors:

1- myocardial ischemia or infarction.

2- intercurrent illness ,e.g infection.

3- arrhythmia, e.g atrial fibrillation.

4- inappropriate reduction of therapy.

5- administration of drug with negative inotropic properties (e.g b- blocker) or fluid retaining properties (e.g non-steroidal anti-inflammatory drugs , corticosteroids) .

6- pulmonary embolism.

7- conditions associated with increase metabolic demand.

8- intravenous fluid overload.[2]

1.1.3- Clinical manifestation:

The presentation of patients with HF includes signs and symptoms of pulmonary congestion, systemic fluid retention, exercise intolerance, or in adequate organ perfusion. Symptoms include dyspnea on exertion, exercise intolerance, orthopnea, paroxysmal nocturnal dyspnea, cough, chest pain that may or may not represent angina, weakness, fatigue, volume overload or pulmonary hypertension, nocturia, insomnia, depression, and weight gain. Patients with end-stage disease may also complain of nausea, abdominal pain, oliguria, confusion, and weight loss. Physical examination findings that should be assessed include jugular venous pressure, wheezing, pleural effusion, displaced point of maximal intensity of P_2 due

to pulmonary hypertension, S_3,S_4, murmurs, hepatomegaly, hepatojugular reflex, low- volume pulses, and peripheral edema. Patients with end-stage disease may also exhibit pulsus alternans, ascites, cool, pale extremities, and cachexia. The symptoms alone can be used to classify the severity of congestive HF and to monitor the effect of treatment, the new york heart association classification(NYHA) is widely used.[3]

Table 1 : NYHA classification of heart failure.

Class I	No limitation of physical activity.
Class II	Slight limitation of physical activity- symptoms with ordinary levels of exertion(e.g. walking up stairs).
Class III	Marked limitation of physical activity- symptoms with minimal levels of exertion (e.g. dressing).
Class IV	Symptoms at rest.

[4]

1.1.4- Investigation:

ECG: usually abnormal; often shows Q waves (previous myocardial infarction) , left ventricular hypertrophy (hypertension), or left bundle branch block (LBBB).

Chest X-ray: cardiac enlargement, congested lung fields.

Echocardiogram: left ventricular dilatation with regional (coronary heart disease) or global (cardiomyopathy) contractile impairment.

Raised B-type natriuretic peptide useful in cases of diagnostic uncertainty.

Renal function is prelude to diuretic and angiotensin converting enzyme (ACE) inhibitor therapy.

Blood count to rule out anemia.

The echocardiogram is the single most important diagnostic test in the patient with heart failure.[5]

If ECG and B-type natriuretic peptide (BNP) are normal, heart failure is unlikely, and an alternative diagnosis should be considered, if either is abnormal, then echocardiography is required. [6]

1.1.5- diagnosis :

heart failure may be diagnosed whenever a patient with significant heart disease develops the signs or symptoms venous congestion . and by Framingham criteria at least 2 major criteria or 1major + 2 minor criteria .

Table 2 : Framingham criteria.

Major criteria	**Minor criteria**
Paroxysmal nocturnal dyspnea, crepitation,S3 gallop, cardiomegaly, increase central venous pressure (>16 cm H2O at right atrium) , weight loss >4.5kg in 5days in response to treatment.	Bilateral ankle edema, dyspnea on ordinary exertion, tachycardia (HR>120), nocturnal cough, hepatomegaly, pleural effusion, decrease vital capacity by 1/3 from maximum recorded.

[6]

1.2- Leukocyte :

Leucocytes are the cells of immune system that are involved in protecting the body against both infectious disease and foreign invaders. All the WBC are produced and derived from multipotent stem cells. Leukocytes are found throughout the body, including the blood and lymphatic system, it divided into the five main types : neutrophils, eosinophil's, basophils, lymphocytes, and monocytes.[7]

1.2.1- lymphocyte :

Are derived from pluripotent hematopoietic stem cells in the bone marrow . there are two main types: T cells (which mediate cellular immunity) and B cells (which mediate humoral immunity). Lymphoid cells that migrate to the thymus develop into T cells , whereas B cells develop in the bone marrow . the majority (about 80%) of lymphocytes in circulation are T cells. [8]

Normal range of lymphocyte is between 1.5 – 3.5 *10^9/L . [7]

1.2.2- Function:

it responsible for adaptive immune response (T and B cells , natural killer cell) it is mediate host defense , modulate the immune response .

The T lymphocytes, after being stimulated, release many cytokines, stimulating macrophages and other cells to destroy the presenting antigen. Cytokines released by T lymphocytes also stimulate the B lymphocytes, eventually leading to the production of antibodies against the antigen causing its destruction.[9]

1.2.3- Causes of lymphocytosis :

1- acute lymphocytic leukemia.

2- chronic lymphocytic leukemia.

3- lymphoma.

4- cytomegalovirus (CMV) infection.

5- HIV/AIDS.

6- mononucleosis .

7- other viral infection.

8- tuberculosis.

9- vasculitis (blood vessel inflammation).[10]

2- Aim :

To define any lymphocyte count abnormalities in patient with chronic heart failure and its relation to clinical presentation.

3- patient and method :

3.1- study design:

A cross sectional study was performed during the period from October 2018 to January 2019 at Al-kadymian teaching hospital, Baghdad, Iraq.

3.2- population:

Inclusion criteria:

This study included a randomly selected 30 patients from in patient ward who were diagnosed to have chronic heart failure based on symptoms and echocardiography. All the patient underwent clinical evaluation including (age, gender, duration of disease, severity of disease and this taken according to NYHA classification of breathlessness , frequency of admission, comorbidity, type of HF, smoking Hx) as well as CBC results including (WBC, lymphocyte count and percentage) in addition to echo parameters EF%, all the patient have informed about the study and give the agree to participation.

Exclusion criteria:

Those people with a predefined cause of lymphocytosis have been excluded, like infection, lymphoma, acute or chronic lymphocytic leukemia .

3.3- Statistical analysis :

Variables described as range and mean $\pm$SD in addition to frequency and percentage using excel10.

4- Results :

The total number of patient in this study was 30 .

The gender distribution showed a female predominance consisting 18 (60%) compared to 12 male (40%) .

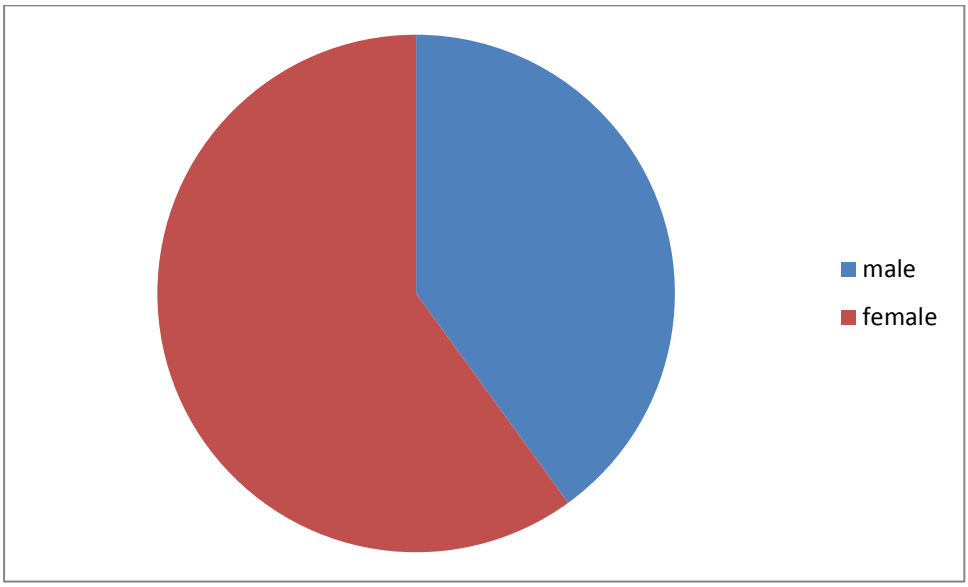

Figure 1 : gender distribution

The age of patient in this study was ranged from(45-86 years old) and the mean age 64.8± 11.29yr , where majority of them >70 years old involved 10 patients as in the table(3) followed by age group 51-60

Table 3 : age distribution

Age yr	Frequency No.	Percentage %	Gender proportion
≤50	3	10%	Male : 2 Female : 1

51-60	9	30%	Male : 3 Female : 6
61-70	8	26.6%	Male : 3 Female : 5
>70	10	33.3%	Male : 4 Female : 6

The duration of HF in these patient is ranged from (0.5- 30 years) and the mean of duration is 4.08± 5.79 yr and the median is 2 yr as in the table(4)

The stage of HF is classified according to NYHA classification , the stage III is the largest group that involved 16 patient (53.3%) as in the table(5)

Table 4 : the stage of HF

Stage	Frequency No.	Percentage %
Stage II	5	16.6%
Stage III	16	53.3%
Stage IV	9	30%

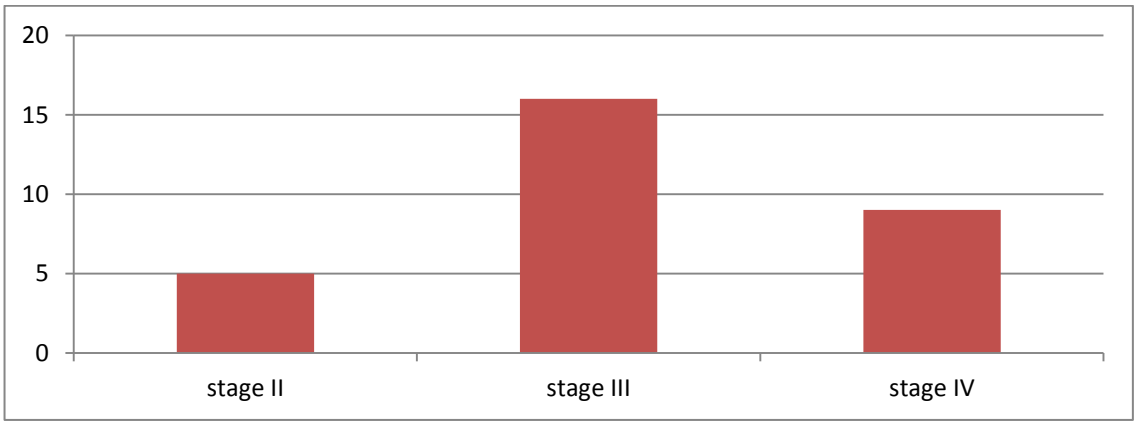

Figure 2 : the stage of HF

Majority had frequent hospital admission 3-6

Table 5 : frequency of admission to hospital

	Frequency No.	Percentage %
<3	10	33.3%
3-6	16	53.3%
>6	4	13.3%

According to the comorbidity of the HF, 17 cases with single disease, 5 with duple disease and 8 with triple disease, the IHD is involved in 22 cases 73.3% , the DM in 16 cases 53.3% and the HT in 13 cases 43.3%.

According to the type of HF the cases with systolic HF is more than diastolic HF as in the table(7)

Table 6 : type of HF

Type of HF	Frequency No.	Percentage %
Systolic	21	70%
diastolic	9	30%

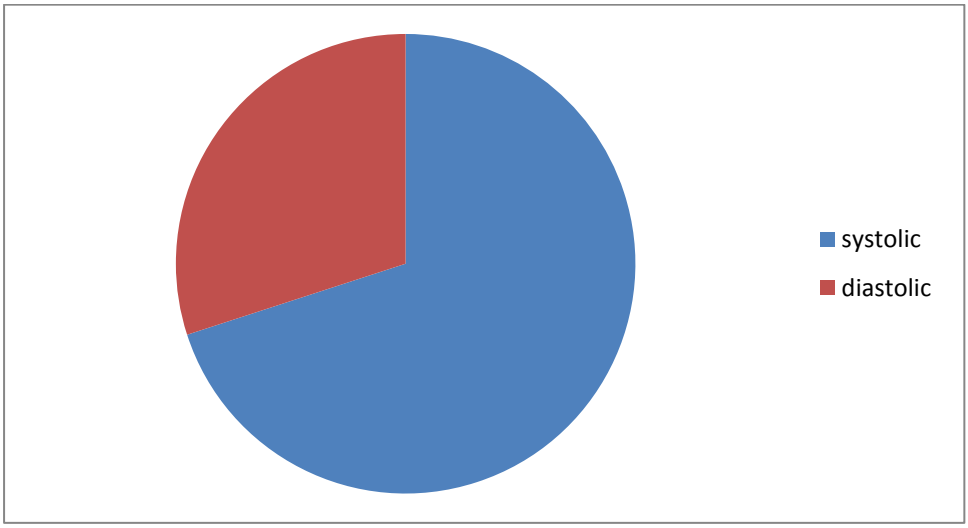

Figure 3 : the type of HF

According to the Echo-EF is ranged between (64%-22%) with mean 47%± 12.78.

Active Smoking history reported in 66% According to the smoking Hx there is 20 cases was negative , the other 10 cases was positive.

Concerning the blood count parameters leukocyte count varied between (4 - 24.5) $x10^3$ /Ml with mean 10.17± 4.56, the lymphocyte count varied between (0.393 – 4.3) $x10^3$/Ml with mean 1.51± 0.99, and the lymphocyte percentage varied between (4.35% - 87.75%) with mean 17.45%± 15.88.

The study showed 12 male, 11 with systolic HF (91.6%) and 1 with diastolic HF (8.3%). 7 with stage 3 (58.3%), 3 with stage 4 (25%), 2 with stage 2 (16.6%).according to smoking Hx, 6 positive, 6 negative.

Table 7 : the distribution of EF, lymphocyte, WBC in male

	min	max	mean	SD
Echo-EF	22%	64%	28%	12.67
Lymphocyte count	0.393	4.3	1.25	1.032
Lymphocyte percentage	5.56%	87.75%	18.28%	22.3
WBC count	4.86	13.6	8.22	3.02

The study showed 18 female, 10 with systolic HF(55.5%), 8 with diastolic HF (44.4%). 3 with stage 2 (16.7%), 9 with stage 3 (50%), 6 with stage 4 (33.3%). According to smoking Hx, 14 negative, 4 positive.

Table 8 : the distribution of EF, lymphocyte, WBC in female

	min	max	mean	SD
Echo-EF	37%	64%	53%	9.23
Lymphocyte count	0.56	3.58	1.68	0.96
Lymphocyte percentage	4.35%	35.8%	16.9%	10.32
WBC count	4	24.5	11.47	5.01

Table 9 : associated of the lymphocyte count with demographic date.

Lym range	No.	Percentage	gender	Mean age	severity	Smoking Hx
1.5-3.5	9	30%	Male:1 Female:8	63± 11.69	Stage II: 1 Stage III: 5 Stage IV: 3	Positive :1 Negative :8
<1.5	19	63.3%	Male:10 Female:9	65.1± 11.8	Stage II: 3 Stage III: 11 Stage IV:5	Positive :7 Negative :12
>3.5	2	6.7%	Male:1 Female:1	70± 0	Stage II: 1 Stage III: 0 Stage IV: 1	Positive :2 Negative : 0

Table 10 : associated of the lymphocyte count with HF.

Lym. rang	EF %
1.5-3.5	52.6± 9.9
<1.5	44.89± 12.42
>3.5	41± 26.8

The study showed 21 cases with systolic HF, 4 with stage 2 (19.04%), 10 with stage 3 (47.6%), 7 with stage 4 (33%). According to smoking Hx, 12 negative, 9 positive.

Table 11 : the distribution of EF, lymphocyte, WBC in cases with systolic HF

	min	max	mean	SD
Echo-EF	22%	55%	41%	10.13
Lymphocyte count	0.393	4.3	1.38	0.988
Lymphocyte percentage	4.35%	87.75%	17.93%	18.37
WBC count	4	19.9	9.57	4.19

The study showed 9 cases with diastolic HF, 1 with stage 2 (11%), 6 with stage 3 (66.7%), and 2 with stage 4 (22%). According to smoking Hx, 8 negative, 1 positive.

Table 12 : the distribution of EF, lymphocyte, WBC in patient with diastolic HF

	min	max	mean	SD
Echo-EF	59%	64%	61%	2
Lymphocyte count	0.56	3.58	1.81	1.02
Lymphocyte percentage	5.20%	28.2%	16.34%	8.35
WBC count	7.5	24.5	11.58	5.309

5- Discussion :

This study showed the mean age is 64.8 ± 11.29 SD which approximated to mean age of the Szygula-jurkiewicz et al study done in the COMMIT-HF registry between 2009-2013, which equal to 61.9± 12.4 SD, and consistent with another study done by Vaduganathan et al on the EVEREST trial with mean age 68.5± 11.4 SD, and also approximated to the study done by Tomohiko sakatani et al in the department of cardiology, matsushita memorial hospital, Osaka, japan, with mean age 72± 12 SD.

According to the gender, this study showed female predominance (60%) and this is approximated to Tomohiko sakatani et al (52%), but differ from Szygula-jurkiewicz et al which is male predominance (76.8%), and another study of vaduganathan et al which is (74.54%) male, because in our country there is low education for use hormonal replacement therapy for post-menopausal women , this lead to increase HF in the female.

According to the severity most of the cases in this study with stage III, IV, and this is correspond to vaduganathan et al, and szygula-jurkiewicz et al, because that all patient is admitted with sever advanced HF, and the sample of study is take from inward patient.

According to the EF, in this study the mean EF is 47%± 12.78 SD, is differ from vaduganathan et al as the mean is 27.3%± 7.9 SD, because in this study the sample is with systolic and diastolic HF and this lead to increase the mean of EF.

According to lymphocyte count and percentage, in this study the mean of count is 1.51± 0.99 SD and the mean of percentage is 17.45%± 15.8 SD, is approximate to the Gideon charach et al in the American journal of cardiology the mean of count is 1.8± 0.7 SD, and consistent with vaduganathan et al the mean of percentage is 21.7%± 9 SD, and to the tomohiko et al the mean of percantage is 24.7%± 8.4 SD, because the HF is lead to poor circulation of the blood and this lead to decrease the production and circulation of the lymphocyte cells in the blood.

6- Conclusion :

* low lymphocyte count is a recognized feature in patient with chronic heart failure

* male patient showed lower lymphocyte count than female.

7- Recommendation :

* we have to study the effect of treatment.

* flow up to detect the prognosis in patient with heart failure and lymphocytopenia.

8- References :

1- D.E. Newby, N.R. Grubb, A. Bradbury. Cardiovascular disease. Stuart H. Ralston, Ian D. penman,Mark W.J. Strachan. Richard P. Hobson. Davidson's, 22nd Edition. Edinburgh London new york oxford phildelphia st Louis; 2014. P. 546-8.

2- Justin A. Ezekowitz, Finlay A. Mcalister, Paul W. anemia is common in heart failure and is associated with poor outcomes: circulation 2003; 107; p. 223-5.

3- Carla S. Dupree. Management of heart failure. Marschall S. Runge, George A. Stouffer, Cam Patterson. Netter's cardiology, 2nd edition; 2004. P. 189.

4- Punit Ramrakha, Jonathan Hill. heart failure. Oxford handbook of cardiology, 2nd edition. United states by oxford university press in new york; 2012. P. 374.

5- Adam D. Timmis, Andrew Archbold. Cardiovascular system. Michael Glynn, William Drake. Hutchison's clinical methods, 23rd edition; 2012. P. 170.

6- James Rudd. Cardiovascular medicine. Murray Longmore, Ian B. Wilkinson, Edward H.Davidson, Alexander Floulkes, Ahmad R. Mafi. Oxford handbook of clinical medicine, 8th edition. United states by oxford university press in new york; 2010. P. 128-29

7- A.V. Hoffbrand, P. A. H. Moss. The white cells. Essential haematology,6th edition. 2011. P. 109- 10.

8- HG Watson, DJ Culligan, LM Manson, haematology and transfusion medicine. Stuart H. Ralston, Ian D. penman,Mark W.J. Strachan. Richard P. Hobson. Davidson's, 23rd edition.

Edinburgh London new york oxford phildelphia st Louis; 2018. P. 917.

9- Barton F. Haynes, Kelly A. Soderberg, Anthony S. Fauci. Introduction to the immune system. Jameson, Fauci, Kasper, Hauser, Longo, Loscalzo. Harrison's principles of internal medicine, 20th edition. New york Chicago san Francisco London; 2018. P. 2451-52.

10- Norman Beck. The leukocytosis. Diagnostic hematology. springer-verlag London limited; 2009.p. 328-29.