



Study Relation of the Fibrinogen and Homocysteine with Coronary Heart Disease

Nasir Kareem Dhahir

Community Health Department, Technical Institute- Baqubah, Middle Technical University, Diyala, Iraq.

Abstract

Because of wide spread chronic infections, especially in patients who have the coronary heart diseases (CHD), and by measuring the inflammatory factors as a biomarker related to this disease including, fibrinogen, homocystein, and the relation of the disease with some risk factors such as the age, blood pressure, body mass index and blood sugar. The study was carried out in the Baqubah teaching hospital in a period from (September/ 2017) to (September/ 2018) in patients who are admitted to coronary care unit (CCU), including (35 patients with myocardial infarction, 24 males , 11 females), and(35 patients with angina pectoris, 19 males, 16 females). The both groups are compared with other healthy group consisting of 20 persons (12 males, 8 females). The range of age was (40-70 years). The principles of method used is by (7 ml) of blood from each patient to estimate the level of serum fibrinogen by using coagulation homeostasis analysis device, and the homocystein is measured by using ELISA technique, and the measuring of the other biochemistry factors by using Cobas Integra 400 plus device. The results of the study showed that, there is a significant value difference $p < 0.05$ of fibrinogen, homocystein, body mass index, systolic blood pressure, fasting blood sugar of patients with myocardial infarction and angina pectoris compared to control (healthy), the levels of the fibrinogen and homocystein will elevated with extreme of the age and increase body mass index (BMI), also there is a positive correlation ($r=0.04$) and in significant value ($p=0.70$) for homocystein and systolic blood pressure, and the correlation ($r=0.08$) in significant value ($p=0.46$) for homocystein and diastolic blood pressure, while the levels of the fibrinogen to systolic blood pressure is($r= - 0.19$) in significant value ($p=0.07$)but the diastolic blood pressure ($r= - 0.09$) in significant value ($p=0.35$). Also there is less positive correlation of fibrinogen to blood sugar ($r=0.039$) in significant value ($p=0.71$) while there is a negative correlation ($r= - 0.04$) in significant value ($p=0.72$) between homocystein and blood sugar. Aim of the study: to investigate the effect of levels of the inflammatory factors involving the fibrinogen and homocystein with relation to coronary heart diseases and study the correlation with other risk factors such as age, blood pressure, body mass index and blood sugar.

Keywords: *Fibrinogen, Homocystein, Coronary heart diseases (CHD), Body mass index (BMI), Myocardial infarction, Angina pectoris, Blood sugar, Cardio vascular diseases(CVD).*

Introduction

The coronary heart disease (CHD) consist of two diseases, the myocardial infarction (MI) also called ischemic heart disease (IHD), and angina pectoris (stable and unstable). It's a disease infect the myocardium duo to coronary artery insufficiency and then less of blood supply to the myocardial muscle.

There are many factors lead to increase the incidence of risk to infect by this disease involved, (age, sex, smoking, obesity, stress, alcohol, hypertension, increase level of the fibrinogen and homocystein) [1, 2]. The WHO (2015) say that the mortality rate number caused by (CHD) in 2012s about 7.4 million

from total of 17.5 million death by cardio vascular diseases (CVD), and 80% from this mortality rate occur in low and middle social economic countries, this percent of mortality is suspect to increase in 2020 duo to coronary heart disease to 11.1 million of dying case [3].

Although a decrease in mortality rate occur caused by cardio vascular disease but there are more than 4 million dying case in Europe alone, 42% of which duo to coronary heart disease (WHO 2012). In the united state the number of patients in coronary heart diseases is about 16 million person, 8 million from which infect by myocardial infarction, it's a

most common disease [3]. In Iraq in spite of many orders present which are restrict mortality statistics but deaths of the cardio vascular diseases are the 1st cause of mortality [4]. Because the wide distribution of the chronic inflammations especially the cardio vascular disease, study the inflammatory factors as a biomarkers on coronary heart disease, which are the fibrinogen, homocystein, and these are connected with other risk factors such as age, body mass index, blood pressure and blood sugar [5].

Fibrinogen have an important role in development of the atherosclerosis from the forming the plaque in to thrombus formation which is the most common cause for the myocardial infarction, the fibrinogen is share in formation the atherosclerosis and thrombus by increase the viscosity of the blood, sedimentation rate of the red blood cells and increase platelets aggregation [6].

But the elevated level of homocysteine (hyperhomocysteinemia) in the blood and increasing atherosclerosis while lead to less blood supply, also the elevated levels of the homocystein in the blood lead to increase thrombosis and by this cause the blood supply in to cardiac muscle is minimized and lead to cardiac attack. Also the increasing of the homocystein lead to high incidence of the deep venous thrombosis by the same method for the development of the atherosclerosis, even the middle level of homocystein can participate in recurrent vascular thrombosis [7].

Aim of the Study

To investigate the effect of the inflammatory factors levels involving the fibrinogen and homocystein with relation to coronary heart disease. Also study the correlation between the fibrinogen and homocystein with the other important risk factors for coronary heart disease involving age, body mass index, blood pressure, blood sugar.

Materials and Methods

The study involved 70 patients was admitted to Baqubah teaching hospital, and divided in to two groups, the 1st group 35 patients have myocardial infarction (24 males, 11 females), the 2nd group 35 patients have angina pectoris (19 males, 16 females), and 20 healthy person as a control (12 males, 8 females).

The range of age is between (40-70 years) and uses the questionnaire form for each patients and healthy person including (age, smoking, sex, systolic and diastolic blood pressure, height, body weight). In a period from September 2017 to September 2018.

The instruments used in the study are to measure the levels of serum fibrinogen, homocystein and glucose, other instruments used are Cobas Integra 400 plus, Centrifuge, Sphygmomanometer, Incubator, Coagulation Haemostasis Analyzer, Ependrof tube, Disposable syringe (5cc), plain tube (10cc), Micropipettes, ELISA system, Balance for body weight measurement, Ruler for height measurement.

Aspirate (7 ml) of blood by disposable syringe and the patient on 12 hours fasting and divided the blood in to three tubes, 2 tubes have 2 ml for each one and 3 ml for the 3rd tube especially for measuring the fibrinogen which contain sodium citrate, and left for 30 min. in a room temperature, and by centrifugation of the 1st and 2nd tubes for 10 min.

For homocystein measurement in 20 C, the normal value of serum homocystein is (1000---2000 nmol/ml,) and also for measure the other biochemical agents by use Cobas Integra 400 plus, the 3rd tube for measure the fibrinogen by using Coagulation Haemostasis Analysis devise after centrifugation for 15 min., the normal value of the serum fibrinogen is (200-400 mg/dl).

Systolic and diastolic blood pressure was measured for each patient by using the sphygmomanometer, also the blood glucose level (fasting blood sugar) was measured by using Cobas Integra 400 plus. By using the height and body weight to exclude the body mass index (BMI) by the formula, body mass index = weight (kg) / height (m²) [8].

Statistics Analysis

Data of current study were analysed by (SPSS version 21 and Excel 2013) programs. (ANOVA) test used to compare between three groups, Pearson correlation (r) used to detect relationship between variables. (ANOVA and Pearson correlation (r) measured by (SPSS) program, while the figures drawing by (Excel 2013). Significant level was at 0.05 ($p \leq 0.05$).

Results and Discussion

In this study there is a connect in levels of the fibrinogen and homocystein as consider as inflammatory factors and biomarker for the

development of coronary heart disease in correlation with risk factors such as the age, body mass index, blood pressure, blood sugar in comparison with control.

Table 1: Levels of the Fibrinogen and Homocystein in Patients with Coronary Heart Disease in comparison with the control

Parameters	Control	Myocardial Infarction patients.	Angina Pectories patients.
Fibrinogen (mg/dl)	39.16 ± 229.59	*117.55 ± 419.47	*136.07 ± 438.56
Homocystein (nmol/ml)	2.62 ± 12.93	*7.78 ± 16.97	*4.9 ± 13.94

* P < 0.05

Table (1) show significant elevation in levels of the fibrinogen in patients of myocardial infarction and angina pectoris in compare with control at a probability level (p=0 < 0.05). This elevations in the fibrinogen in patients of myocardial infarction and angina pectoris consider as a risk factor for happiness of the CHD and it is participate to increase the blood viscosity in cases of the inflammations duo to cardiovascular diseases CVD especially CHD [10, 11]. There is strong relation between the fibrinogen and coronary artery diseases and plaque formation by connect the fibrinogen with risk factors who related to

cardiovascular diseases in both sexes [12, 13]. Also there is a significant differences in levels of the homocystein in patients with myocardial infarction and angina pectoris in a probability level (p= 0.05). Any increase in the level of homocystein make the cells more prone to infect and lead to vascular inflammation and develop to atherosclerosis and the net result is the ischemic injury, for this cause the elevation of the homocystein consider as probable risk factor for coronary artery diseases by formation of the atherosclerotic plaque, blood clot and ischemic heart disease [14].

Table 2: Incidence of Special Risk Factors for Coronary Heart Disease in Compare to Control

Parameters	Control	Myocardial infarction	Angina pectories
Patients Number	20	35	35
Sex(male / female)	12 / 8	24 / 11	19 / 16
Age (years)	5.74 ± 51.1	* 9.29 ± 56.6	* 8.74 ± 60
Body Mass Index (kg/m ²)	1.12 ± 25.92	4.06 ± 26.96	* 4.70 ± 29.15
Systolic Blood Pressure(mm/Hg)	8.29 ± 115.24	*22.16 ± 137.13	*21.69 ± 134.84
Diastolic Blood Pressure(mm/Hg)	6.33 ± 74.74	*15.62 ± 88.07	*14.63 ± 83.13
Fasting Blood Sugar (mg/dl)	89.50 ± 99.52	*103.68 ± 165.19	*88.42 ± 176.10

* P < 0.05

Table 2: Shows there are significant differences in the range of ages of patients who have myocardial infarction and angina pectoris compare to control. This significant differences have a major effect on development of the CHD because the age is

consider as an independent risk factor in connected with other risk factors for CVD [15]. Also there is positive correlation (r=0.13) and a probability level (p=0.21) between levels of the fibrinogen and the age as shown in Figure 1.

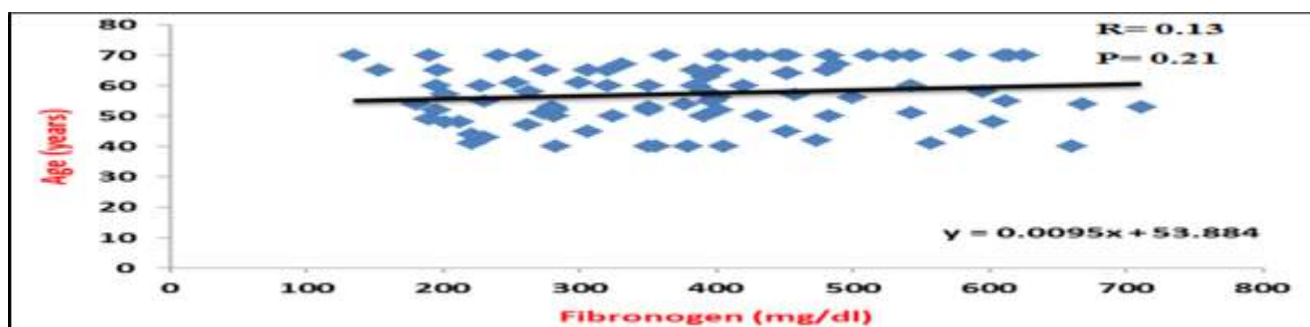


Figure 1: The Relation between the Fibrinogen and the Age

The level of fibrinogen gradually increase with advance of the age, and will lead to increase platelets aggregation and clotting factors with decrease in levels of the clotting inhibition and then decrease the fibrinolysis [16]. While the advance in the age elevate the levels of the homocystein in the blood and

lead to develop the blood vessels disease through the effect on the platelets, clotting factors and dysfunction endothelial layer [17]. The correlation between the homocystein and the age is positive ($r= - 0.002$) and probability level ($p=0.98$) as shown in Figure 2.

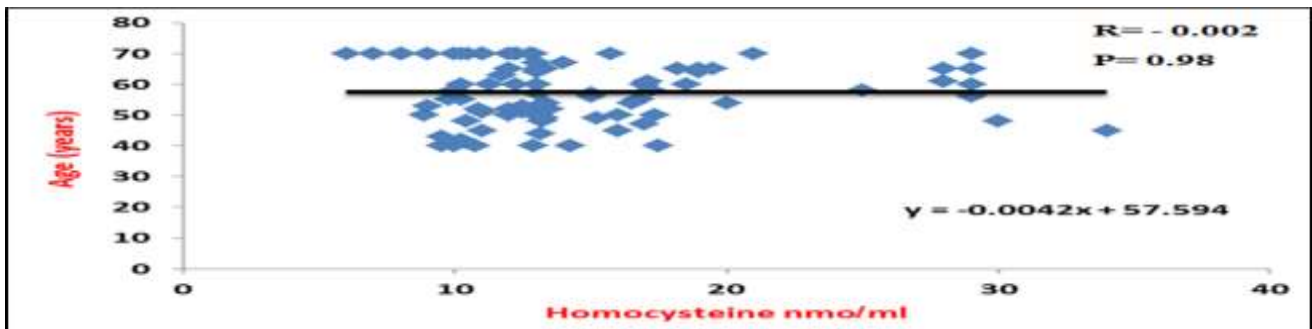


Figure 2: The Relation between the Homocystein and the Age

Also from the table 2 the body mass index in patients with myocardial infarction and angina pectoris reach (4.06 ± 26.96), (4.70 ± 29.15) kg/m^2 , this mean the patients of myocardial infarction have morbid obesity while the patients of the angina pectoris have obesity only, there are many studies say that the obesity is one of the major risk factor for the coronary heart disease, from this the risk factors will increase and decrease with high and low body mass index [18, 19]. The obesity play a major role in opposite effect on risk

factors of the CHD such as hypertension, dyslepdemia and the diabetes mellitus consider as a major element for the metabolic syndrome and probably it is independent risk factor to occur the coronary heart disease and atherosclerosis [20]. There is a positive correlation ($r=0.29$) in significant level ($p=0.006$) between the levels of the serum fibrinogen and BMI, the level of fibrinogen will elevated with increase the body mass index (Figure 3). Also increase after menopause [21].

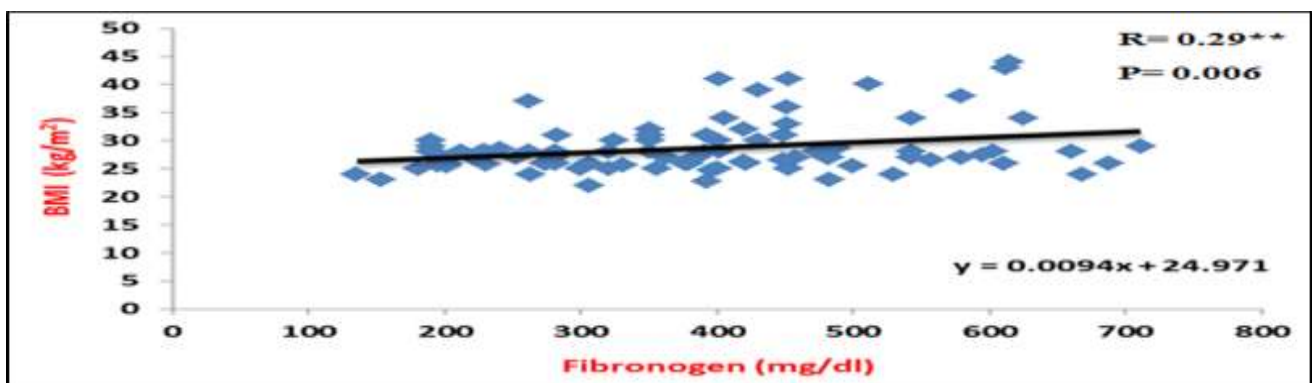


Figure 3: The Relation between the Fibrinogen and Body Mass Index

While there is less correlation between the homocystein and the body mass index ($r=$

0.23) and probability level ($p=0.02$) as in Figure 4.

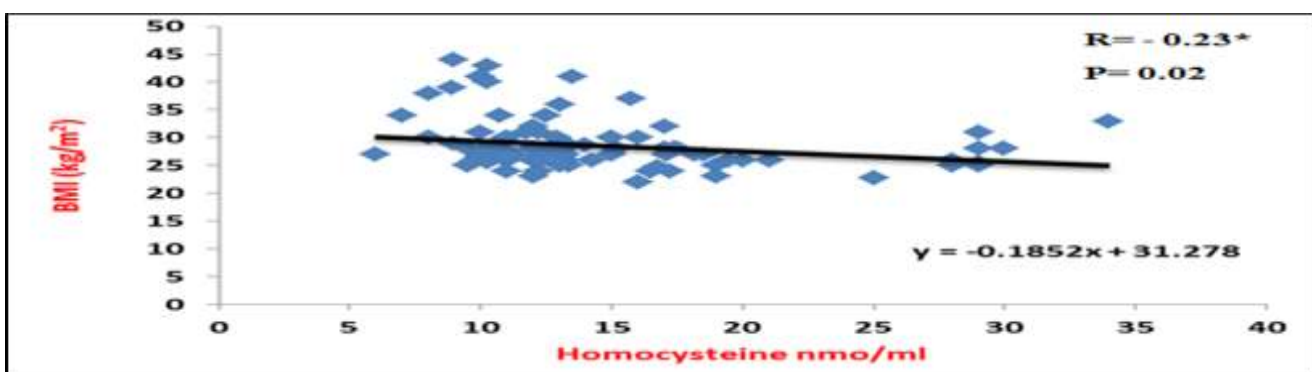


Figure 4: The Relation between the Homocystein and Body Mass Index.

The study appear there is a significant differences in a probability level $p < 0.05$ in value of the systolic blood pressure between groups of the myocardial infarction and angina pectoris compare to control. While the values of the diastolic blood pressure in the same groups of patients appear increase significant value at probability level $p < 0.05$ compare to control. The Amarecan Heart Association (AHA) appears in their yearly

reports in 2004 the blood pressures consider is one of the important risk factors for developing the CVD and the atherosclerosis [22]. While the relation between the fibrinogen and systolic blood pressure ($r = -0.19$) in probability level ($p = 0.07$), and the relation with the diastolic blood pressure ($r = -0.09$) in significant level ($p = 0.39$) as in Figures 5 and 6.

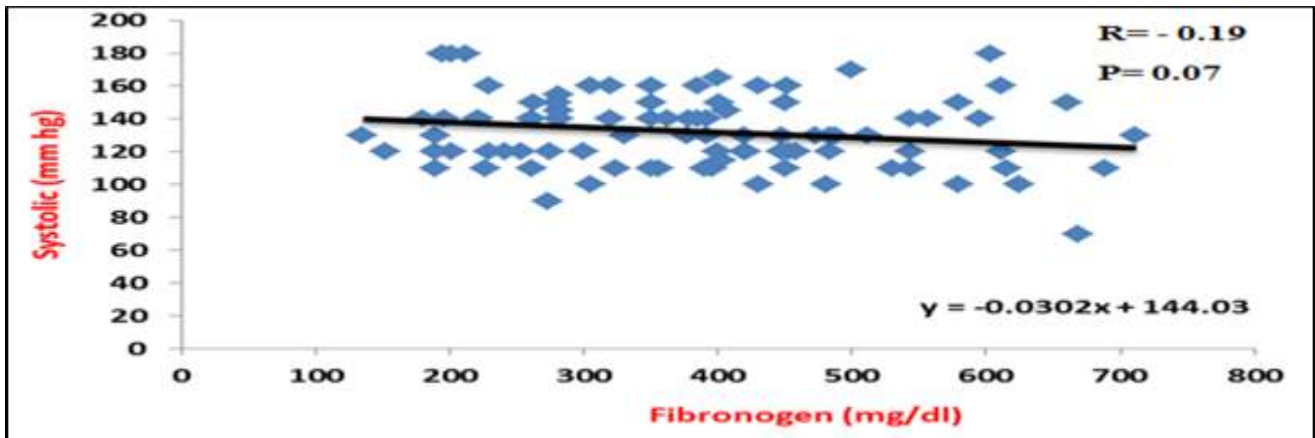


Figure 5: Relation between the Fibrinogen and Systolic Blood Pressure

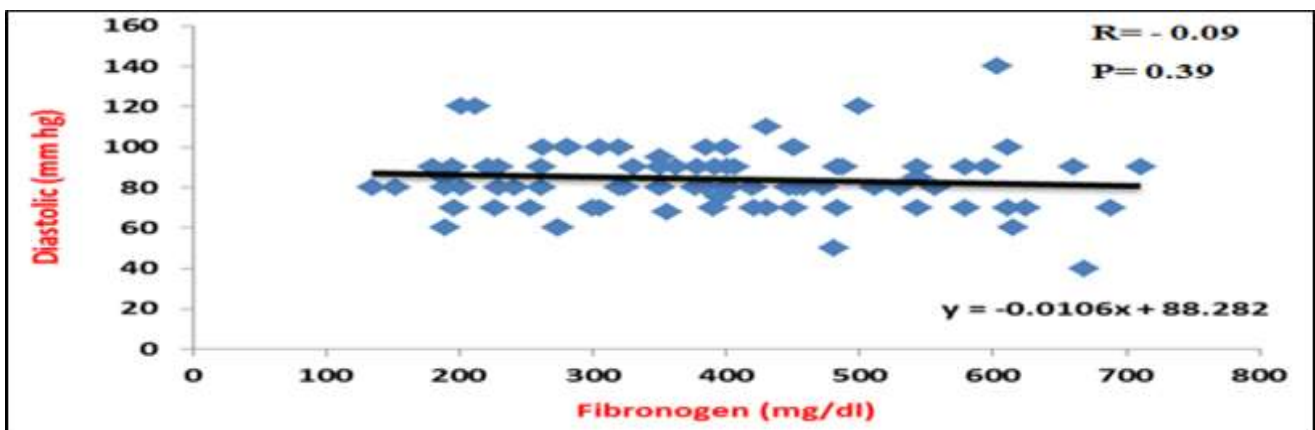


Figure 6: Relation between the Fibrinogen and Diastolic Blood Pressure

Also the study results there is positive correlation ($r = 0.08$) in significant level ($p = 0.46$) between the homocystein levels and diastolic blood pressure, and there is

correlation of ($r = 0.04$) in significant level ($p = 0.71$) between the homocystein levels and systolic blood pressure as in Figures 7 and 8.

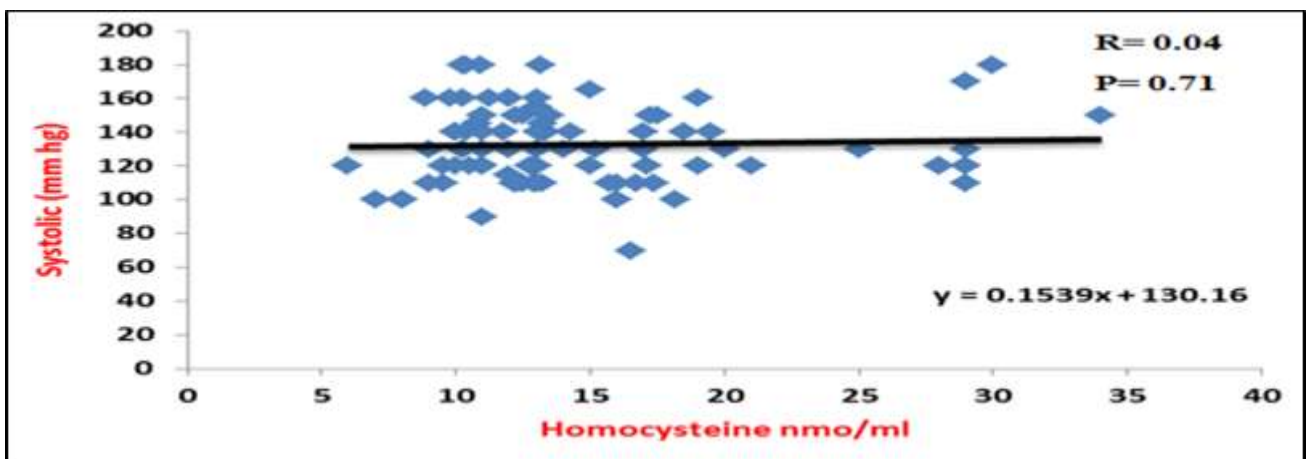


Figure 7: Relation between the homocystein and systolic blood pressure

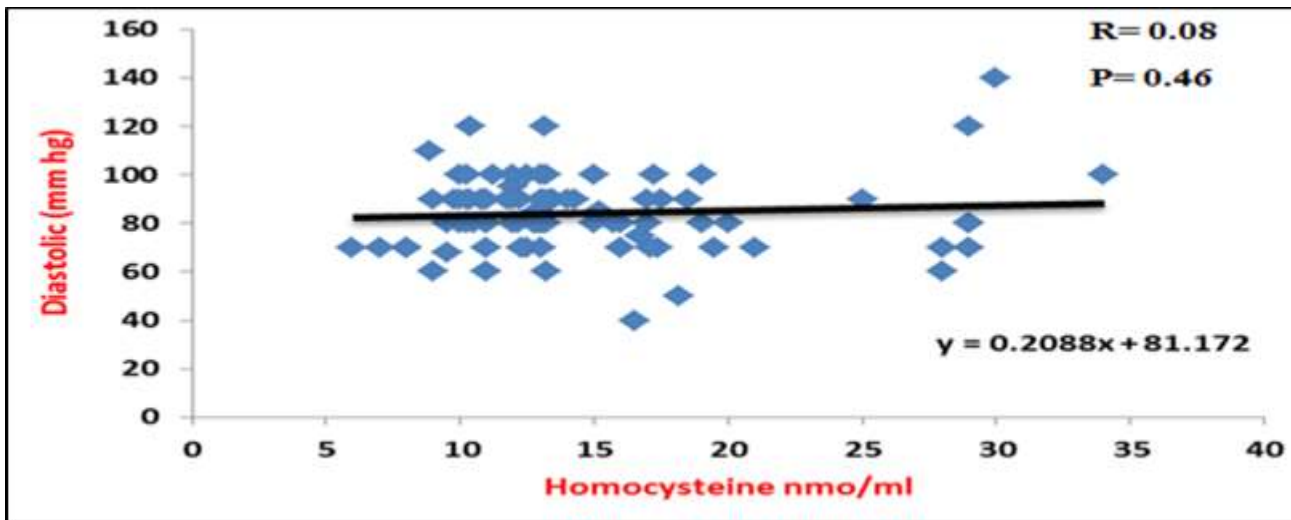


Figure 8: Relation between the homocystein and Diastolic Blood Pressure

From table 2 there is increase in significant value $p < 0.05$ in levels of the fasting blood sugar in groups of the myocardial infarction and angina pectoris who had diabetes mellitus compare to control. But there is no significant differences between the

myocardial infarction and angina pectoris. The relation between the blood glucose and the fibrinogen, there is low positive correlation ($r=0.04$) in probability level ($p=0.71$) as in Figure 9.

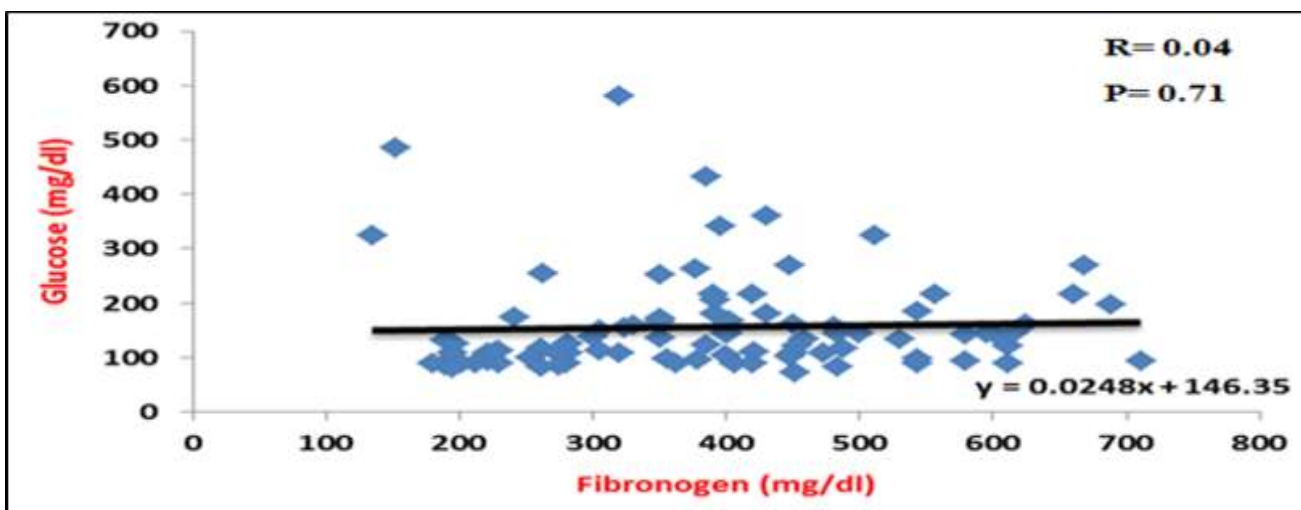


Figure 9: Relation between the Fibrinogen and Blood Glucose

While there is positive correlation ($r=-0.04$) in a probability level ($p=0.72$) between the

homocystein and blood glucose as in Figure 10.

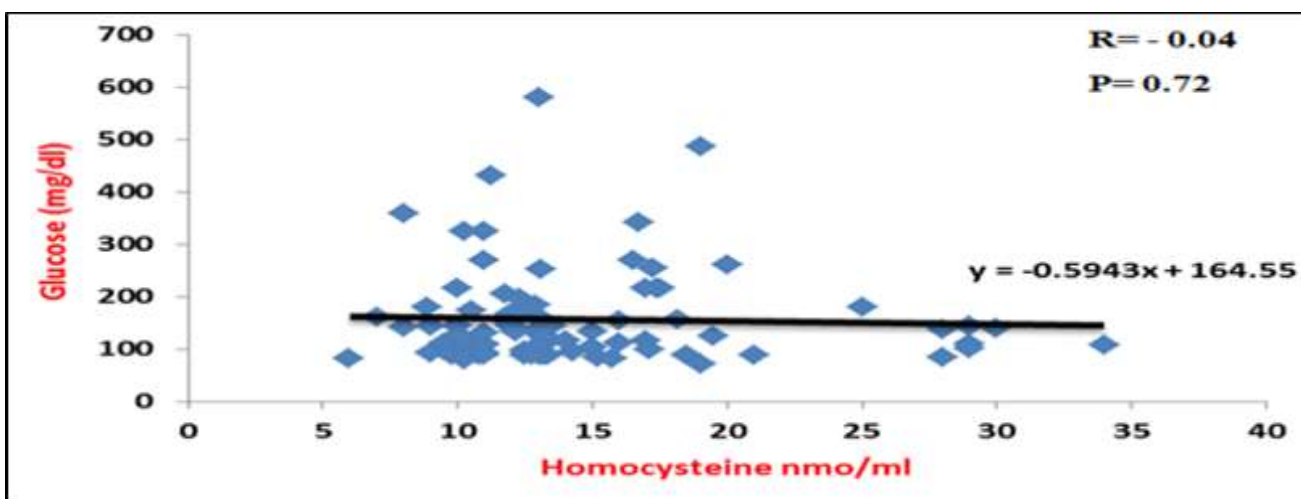


Figure 10: Relation between the homocystein and blood glucose

References

1. AL-Dileamy BN, AL-Obeidy ES (2009) HLA prevalence in Iraqi patients with ischemic heart disease. *J. Fac. Med. Baghdad*, 52 (2): 2010.
2. Al Jubawii AA, Al-Humairi AK, Ali MH (2016) Incidence of Ischemic Heart Disease among Patients with Mitral Annulus Calcification in Babylon Province. *Journal of Babylon University/Pure and Applied Sciences*, 5: 24.
3. American Heart Association (AHA) (2004) International C.V. disease statistics. Dallas. American Heart Association
4. Ala'din A (2004) MD, FRCP, FFPH, Ministry of Health Second Edition, December.
5. Jialal I, Verma S, Devaraj S (2009) Inhibition of endothelial nitric oxide synthase by C-reactive protein: clinical relevance. *Clin Chem.*, 55: 206-8.
6. Bembde AS (2012) A Study of Plasma Fibrinogen Level in Type-2 Diabetes Mellitus and its Relation to Glycemic Control. *Indian J. Hematol. Blood Transfus.*, 28(2):105-108.
7. Michael LG, Genest JJ, Rosen R (2006) Elevated homocysteine reduces Apo lipoprotein A-I expression in hyperhomocysteinemic mice and in males with CAD. *Circulation Res*, 98: 564- 571.
8. Swash M (2002) Hutchisons Clinical Methods, 21 st edition, W.B. Saunders.
9. Ridker PM, Hennekens CH (2000) *N. Eng J. Med.*, 342: 836-43.
10. Ang LKB, Ilapakurtti TM, Mahmud E (2013) Elevated plasma fibrinogen rather than residual platelet reactivity after clopidogrel pre-treatment. *Journal of the American College of Cardiology*, 61 (1): 23-34.
11. Luca GD, Verdoia M, Bolzani V, Marino P (2010) High fibrinogen level is an independent predictor of presence and extent of coronary artery disease among Italian population. *J. Thrombol.*, 10:1007.
12. Shojaie M, Pourahmad A, Izadi HER, Naghshvar F (2009) Fibrinogen as a risk factor for premature myocardial infarction in Iranian patients: *Vascular Health and Risk Management*, 5: 673-676
13. Braun NSG, King L, et al (2013) Relation of fibrinogen level with cardiovascular events in patients with coronary artery disease. *American Journal of Cardiology*, 111 (6): 804-810.
14. Bostom AG, Shemin D, Dworkin L, Selhub J (2000) Treatment of mild hyper homocysteinemia in renal transplant recipients versus Hemodialysis patients. *Transplantation*, 69(10): 2128-31.
15. National Center for Health Statistics (NCHS). United States (2010) with special feature on death. Washington DC: US Government Printing Office. Available from: <http://www.cdc.gov/nchs/data/hus/hus10>.
16. Ali MA, Al-Ghany HA, Jalil HN (2013) The Relationship between Fibrinogen Level and very High Parity. *Iraqi J. Comm. Med.*, 1.
17. Didit D (2014) Food and nutrient associated with vitamin B12 biomarkers among vegetarian and non-vegetarian participants of the Adventist health study. School of Public Health. Thesis .calibration study.
18. McGee DL (2005) Body mass index and mortality: a meta-analysis based on person-level data from twenty-six observational studies. *Ann Epidemiol.*, 15:87-97
19. Whitlock G, Lewington S Halsey, Qizilbash N, Collins R, Peto R (2009) Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. *Lancet*, 373:1083-1096
20. Zhang PD, Cheng Z, Yan C, Choi ET, Han Y, Wang H (2014). Hyperhomocysteinemia Potentiates Hyperglycemia Induced Inflammatory Monocyte Differentiation and Atherosclerosis. (*Diabetes*), 63:4275-4290 | DOI: 10.2337/db14-0809
21. Kafle DR, Shrestha P (2010) Study of fibrinogen in patients with diabetes mellitus. *Nepal Med Coll. J.*, 12(1):34-37.
22. Chobanian AV, Bakris GL, HR Black et al (2003) Evaluation, and treatment of high blood pressure Hypertension, 42: 1206-1252.