Relation of angiography to hematological, hormonal and some biochemical variables in coronary artery bypass graft patients

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Abstract The present study was designed to investigate the relation between severity of atherosclerosis via angiography and alteration of some important biochemical, hormonal and hematological variables in patients underwent Coronary Artery Bypass Graft (CABG) surgery. Eighty adult patients underwent coronary angiography were included in this study, and a standardized case-control study of acute myocardial infarction was established through taking 20 healthy individuals. Diagnostic coronary angiography was performed by a team of expert cardiologists. The patients were grouped according the number of major epicardial coronary arteries into one vessel disease (1VD), two vessels disease (2VD) or three vessels disease (3VD). The evaluation of biochemical tests were performed. The results of association of measurements with the severity of disease showed the priority of cholesterol and its related indexes (especially LDL) rather than TG indicating the severity of atherosclerosis. While, blood glucose and HbA1c were not apparently related to the degree of atherosclerosis. Significant reduction of T3 hormone and platelets and elevation in MPV were recorded in patients suffering from three vessels occlusion. This finding suggested strong association between severity of atherosclerosis and LDL, MPV and T3 in CABG patients.

Key words: CABG, Atherosclerosis, angiography, laboratory findings

1. Introduction
Coronary heart diseases (CHD) is the leading cause of death worldwide, accounting for 17.3 million death per year. This data is predicted to reach over 23.6 million by 2030 [31]. WHO has reported that out of 1 in 7 death in 2015 were occurred as a result of chronic heart disease[30]. CHD is a disease caused by atherosclerosis or having waxy plaque within the coronary arteries, which results in
constriction of blood flow to the heart. Patients may experience stable angina or remains asymptomatic until occurrence of thrombosis, which may leads to Myocardial infarction (MI) [19]. Coronary artery bypass grafting (CABG) is a type of surgery that improves blood flow to the heart. Surgeons use CABG to treat people who have severe (CHD). Surgeons can bypass multiple coronary arteries during one surgery [32]. Compute tomography Coronary Angiography (CTCA) visualizes and scans the details of blood vessels throughout the coronary arteries. It provides the X-ray anatomical image of the arteries that supply blood to the heart. If appropriately performed, CTCA can be considered as a reliable method for coronary artery visualization, with a high negative predictive value for the exclusion of significant coronary artery stenosis [4, 29]. Several laboratory findings, especially serum lipid and lipoprotein related investigations are recognized as important risk factors for detection of the presence and severity of CAD. In a study on Chinese high-risk patients, among all the metabolic syndrome components, elevated waist circumference, reduced HDL-C, and elevated fasting glucose might have the relatively higher association with CAD, whereas elevated TGs and elevated blood pressure might have weaker association [16]. Epidemiological studies indicated that hyperglycemia plays an independent role in cardiovascular disease[3]. Hyperglycemia, regardless of diabetic status, remains to be a risk factor for the short-term mortality of patients with acute myocardial infarction and treated with percutaneous coronary intervention [21].

Thyroid hormone mediates the expression of both structural and regulatory genes in the cardiac myocyte [9], even mildly altered thyroid status affects serum cholesterol levels [8], which increase the risk of coronary artery disease [6, 18, 39]. Moreover, PLTs have been shown to produce several inflammatory mediators and growth factors that play a role in atherothrombosis [1].

In spite of several previous studies on the impact and association of laboratory tests with CAD, many laboratory tests remained as a matter of study to be regarded as risk factor for CHD or not. Therefore, The main goal of this study is finding the association between the severity of the attack with the level of some laboratory findings related to glucose, lipid and thyroid functions, and hematological variables.

2. Materials and Methods
2.1. Patients and Sampling process
Data was collected from a total of 80 adult CABG patients underwent coronary angiography at Erbil Cardiac center. Patients age’s matches (45-80) years and their weight range was (65-105 kgs). The whole history was obtained from all patients using prepared questionnaire. We established a standardized case-control study of acute myocardial infarction through taking 20 control healthy individuals.

2.2. Blood samples collection
Blood samples were taken from peripheral veins by 10 ml vacutainer. Three mL of blood samples was immediately transferred to ethylenediaminetetraacetate (EDTA) specimen bottles for measurement of hematological parameters, 7 ml put into clot activator tube for serum separation. Serum was separation by 3000 round per minute (rpm) centrifugation for 15 min.

2.3. Angiography
Diagnostic coronary angiography (CAG) was performed by a team of expert cardiologists. A detailed analysis of angiographic was done by the operators. Both eyeballing method and quantitative coronary angiography (QCA) were used to estimate the percentage, morphology and length of the coronary lesions. The patients were grouped according the number of major epicardial coronary arteries into one vessel disease (1VD), two vessels disease (2VD) or three vessels disease (3VD).
2.4. Thyroid function tests (T3, T4 and TSH)
Elecsys Triiodothyronine (Triiodothyronine T3, Thyroxine T4 and Thyroid stimulating hormone TSH) reagent ready kits were used on cobas e411 immunoassay analyzers.

2.5. Hematological Measurements
Estimation of total Leukocyte counts (WBCs), Eosinophil, hemoglobin (Hgb), hematocrit (Hct) mean platelet volume(MPV) , and platelets (PLT) variables were made using ‘Hemolyzer 5’Analyzer. While estimation blood sugar and HbA1c made by cobas c311 biochemistry analyzer.

2.6. Estimation total Cholesterol, Triglycerides, LDL-Cholesterol and HDL-Cholesterol
The amount blood sample on collected in activator tube, Centrifuge samples containing precipitates before performing the assay. After obtained pure serum put 1ml serum into cuvette on the disk for running the sample aspirated serum for each one needed 2 L only HDL needed 2.5 L. The analyzer automatically calculated the analyte concentration of the sample in mg/L.

2.7. Statistical analysis
Graphpad Prism version 6.01 was applied for performing statistical analysis. Unpaired t test and one-way ANOVA were used for comparison between treatments. Tukey test was applied as post hoc test for ANOVA results, and all data were expressed as mean and standard error of the mean.

3. Results
The clinical characteristics for the patients (Table 1) recorded high significant elevation (P<0.0001) of measures related to diabetes including blood sugar and HbA1c percent. Lipid profile of the patients were within the normal range, however of significant differences regarding the bad cholesterol variables such as LDL, serum total cholesterol and Non-HDL cholesterol with control group. Thyroid function tests and hematological measurements were also within the normal range, in spite of significant difference of almost all parameters comparing to control except for T4 and HGB level.

Table 1. Clinical characteristics of CABG patients comparing to control healthy individuals.

| Clinical Characteristics | Patients Mean ± SEM | Control Mean ± SEM | Sig. (P value) |
|--------------------------|---------------------|--------------------|---------------|
| Blood Sugar (mg/dl)      | 185.70 ± 12.06      | 104.13 ± 2.94      | P<0.0001      |
| HbA1c %                  | 7.57 ± 0.24         | 5.04 ± 0.10        | P<0.0001      |
| S. Cholesterol (mg/dl)   | 158.79 ± 4.49       | 138.47 ± 5.23      | P<0.05        |
| Non-HDL Cholesterol (mg/dl) | 122.25 ± 3.48     | 100.20 ± 3.68      | P<0.05        |
| S. TG (mg/dl)            | 177.92 ± 9.58       | 139.57 ± 11.90     | P<0.05        |
| HDL-C (mg/dl)            | 36.54 ± 1.01        | 38.27 ± 1.56       | NS*           |
| LDL-C (mg/dl)            | 99.30 ± 3.98        | 80.47 ± 4.25       | P<0.05        |
| T3 (nmol/L)              | 1.57 ± 0.04         | 1.76 ± 0.07        | P<0.05        |
| T4 (nmol/L)              | 106.26 ± 2.08       | 107.73 ± 3.92      | NS            |
| TSH (μIU/ml)             | 2.41 ± 0.30         | 1.85 ± 0.20        | P<0.05        |
| WBC (10³/μL)             | 8.64 ± 0.27         | 6.61 ± 0.31        | P<0.001       |
| Eosinophil %             | 0.17 ± 0.02         | 0.31 ± 0.02        | P<0.001       |
| HGB (mg/dl)              | 14.34 ± 0.16        | 14.13 ± 0.26       | NS            |
| Platelet count (10³/μL)  | 227.68 ± 5.93       | 275.43 ± 8.46      | P<0.05        |

*NS indicates non-significant differences

Figure 1 shows the association between the severity of atherosclerosis (represented by the number of artery as one, two, three or occluded arteries beside the control healthy arteries) with biochemical
parameter (lipid profile). Total serum cholesterol showed significant differences between control, mild, moderate and severe atherosclerosis with mean values (163.1±7.08 mg/dL), (150.8±6.54 mg/dL), (171.6±9.23 mg/dL) and (124.0±18.8 mg/dL) respectively. A clear elevation of S. Cholesterol was observed with increasing the number of occluded arteries which indicates the importance of cholesterol estimation.

The level of serum triglyceride increased significantly (p<0.05) with the increasing the degree of severity of atherosclerosis with mean value (157.0±11.9 mg/dL), (192.7±18.27 mg/dL), (191.6±17.6 mg/dL) and (112.6±29.9 mg/dL) respectively as shown in figure 1. However, the elevation of TG in different degrees was not significant. The non-significant differences in the S.HDL, while the results of S.LDL levels were demonstrated to be significant at p<0.05 and it was similar to the results mentioned in serum cholesterol as it is derived from it, as illustrated in Figure 1.

Figure 1. The association between the severities of coronary artery diseases (represented by the number of artery) with lipid profile of the patients. The level of total serum cholesterol showed non-significant difference between the groups (p<0.05). The level of serum triglyceride recorded significant difference between the groups. The level of S.HDL & S.LDL was non-significant between the groups. All the data represented as mean ± S.E and one-way ANOVA and Tukey post-hoc were performed for comparison among them. *(a,b,c) Same letters mean non-significant differences, while different letters indicate significant differences*

Figure 2 presents the association between BG and HbA1c with the severity of coronary artery diseases, represented by single vessel diseases, two vessels diseases, and three vessels diseases compared to control. The results indicated that blood glucose and the level of HbA1c were not changed statistically in different
groups of CABG patients of the study. However, there were significant differences between the control group compared to all three groups of patients.

A clear declining in the level of T3 was reported with increasing the number of stent coronary arteries (Figure 3). Thereby, hypothyroidism could be related to the increasing the severity of atherosclerosis. Despite reduction of T4 and induction of TSH secretion with increasing the number of occluded arteries, but the comparison suggested the differences to be non-significant.

Figure 4 illustrates the comparison between the degree of atherosclerosis regarding WBC and Eosinophil count. The level of WBCs was non-significantly differences present with mean values (8.45± 0.56 103/μL), (8.85 ± 0.50 103/μL), (8.57 ± 0.39 103/μL) and (8.43±1.02 103/μL) (P<0.05).
of eosinophil was non-significant differences between groups with mean values (0.178±0.045 %),(0.194±0.048 %),(0.162±0.030 %)and (0.112±0.053 %)with p-value(p<0.05).

Figure 5. association between the severities of coronary artery diseases (represented by the number of artery). The level of WBCs showed non-significant difference between the groups with (p<0.05). The level of eosinophil was significant between control and all groups of patients (p<0.05). All the data represented as mean ± S.E and one way ANOVA and Tukey post-hoc were performed for compassion among them. * (a,b,c) Same letters mean non-significant differences, while different letters indicate significant differences

Figure 6. the association between the severity of coronary artery diseases compared to control. (A)The level of hemoglobin was significantly differences present with mean values (14.2± 0.24 g/dL), (15.1 ± 0.23 g/dL), (13.4 ± 0.22 g/dL) and(14.8±0.78 g/dL) (P<0.05).

Figure 6. association between the severities of coronary artery diseases (represented by the number of artery). The level of HGB and MPV showed significant difference between the groups with (p<0.05), the significant differences is clearly appeared in three vessels disease (3VD). The level of platelet also showed significant difference between the groups with (p<0.05). All the data represented as mean ± S.E and one-way ANOVA and Tukey post-hoc were performed for compassion among them. * (a,b,c) Same letters mean non-significant differences, while different letters indicate significant differences
Figure 7 the association between the severity of coronary artery diseases (represented by the number of artery) single vessel diseases, two vessels diseases, and three vessels diseases compared to control. The level of platelet was significantly differences present with mean values $(252.2 \pm 10.4 \times 10^3/\mu L)$, $(222.7 \pm 11.4 \times 10^3/\mu L)$, $(216.1 \pm 8.33 \times 10^3/\mu L)$ and $(212.0 \pm 22.0 \times 10^3/\mu L)$ ($P<0.05$). Also the level of MPV was non-significant differences between groups with mean values $(8.22 \pm 0.31 \text{ fL}), (8.56 \pm 0.23 \text{ fL}), (8.95 \pm 0.275 \text{ fL})$ and $(9.20 \pm 0.38 \text{ fL})$ with $p$-value($<0.05$).

4. Discussion

The present investigation proposed the possible relation between the severity of atherosclerosis indicated by angiography with alteration of common biochemical and hematological variables including (Lipid profile, Thyroid function tests, Blood Glucose, HbA1c, RBC related parameters, WBC and platelet variables) estimated in patients underwent coronary bypass graft surgery. The results concluded that there is a clear gradient of the risk of coronary heart disease by Cholesterol and TG levels. Persons with high cholesterol levels being at higher risk than persons with low levels. [15].

The association between plasma total cholesterol (or LDL and Non-HDL cholesterol) and CHD risk is well established. Thus, epidemiological evidence supports the view that LDL cholesterol is important in atherosclerosis development.[22]

Our data support the suggestion that diabetic patients without previous myocardial infarction have as high a risk of myocardial infarction as nondiabetic patients with previous myocardial infarction. These data provide a rationale for treating cardiovascular risk factors in diabetic patients as aggressively as in nondiabetic patients with prior myocardial infarction.[17]. However, it has been found that diabetic individuals who have accelerated atherosclerosis, and hyperglycemia has been shown to relate subsequent new arterial diseases, but not as truly independent risk factors [12], this relation could be explained by Insulin resistance and its attendant metabolic abnormalities which may cause much of the increased cardiovascular risk of diabetes.[27]

In addition, the cumulative oxidative stress of chronic ischemia may be additive to the oxidative stress superimposed by diabetes. This oxidative stress results in myocardial subcellular remodeling, leading to abnormal intracellular calcium homeostasis.[10]. DM-associated atherosclerosis can lead to complications in all major of vascular beds, including the coronary arteries, carotid vessels, and lower extremity arteries [13, 28]. For example, a study by [17] estimated the 7-year incidence of a first-time myocardial infarction (MI) in diabetic patients at 20.2%, compared to 3.5% in nondiabetic patients.

On the other hand, thyroid hormone excess increases oxygen demand and cardiac work and induces tachyarrhythmias, particularly atrial fibrillation, coronary spasm, and cardiac ischemia even in the absence of significant coronary artery disease[7]. Generally, T3 increases the force and speed of systolic contraction and the speed of diastolic relaxation.[25] In addition, T3 decreases vascular resistance, including coronary vascular tone, and increases coronary arteriolar angiogenesis.[25]

Our study reported that MPV changed between patients with CAD and those with normal coronary arteries. However, studies Shown MPV as an independent for prognosis in patients with cardiovascular diseases such as myocardial infarction (MI).[34, 35], which is agree to our study results. It has been suggested that mean platelet volume (MPV) is increased during acute myocardial infarction.[23], While, in some studies results failed to demonstrate a difference in mean platelet count between patients with coronary arteries diseases and those with normal coronary arteries.[20]. These inconsistent results may be
due to variability in their research methodologies and/or individual differences in vulnerability to SD that have resulted in such disparities.

In the present study, patients group had a significantly highly WBC count than healthy controls. This finding is compatible with rise in WBC which was evident even after acute myocardial infarction[38]. This acute response might represent a catecholamine and cortisol effect, which mobilizes neutrophils from the marginated granulocyte pool.[2, 11, 26]. Therefore, the elevation of WBC count in acute MI patients mainly due to increased neutrophils.[1]

Our study reported that eosinophil was low in patients with myocardial infarction compared with healthy controls. Parallel to our study, Eosinophil$^\%$ in patients with AMI was significantly lower when compared with controls, suggesting that eosinophils are attracted to the site of the lesion soon after the thrombotic event. Eosinophils may be recruited to that site via complex interactions with soluble factors and cell contacts, mostly mast cell-mediated.[14]. In addition to the increased WBC counts, these cells may also be activated in AMI [33].

Several previous studies have proposed the reduction of platelets count in cases related to CVD [5, 24]. The decreased the level of platelet that are execute in a diversity of state leads to inflammation.

Our findings was similar to [36] that the level of triglyceride was associated with severity of atherosclerosis and increased wall thickness and progressive plaque formation. Though, Hyperlipidemia is another risk factor that favor the development of CVD [37].

5. References

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