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Relation of Cardiovascular Risk Factors with Coronary Angiographic Findings in Iraqi Patients with Ischemic Heart Disease

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Abstract **Background:** Atherosclerotic coronary artery disease is a major cause of death all over the world. Among patients with coronary artery disease, there are different cardiovascular risk factors which may exhibit their effects on coronary angiographic findings. This work aimed to study the relation of different cardiovascular risk factors with coronary angiographic findings in patients with ischemic heart disease (IHD). **Methods**: This case-series prospective study involved 220 patients with IHD who underwent coronary angiography in Mosul Cardiac Catheterization Unit in Ibn-Sina Teaching Hospital over a period of five months from April 1st through August 31st 2006. Patients with different coronary risk factors including smoking, positive family history of IHD, type 2 diabetes mellitus (T2DM), hypertension (HT), dyslipidemia, obesity and physical inactivity who presented with IHD were categorized and compared according to presentations into; ST-elevation myocardial infarction (STEMI) (n = 72), Non-ST-elevation myocardial infarction (NSTEMI) and/or unstable angina (n = 98) and chronic stable angina (n = 50) and then the patients were re-grouped according to the number of cardiovascular risk factors into patients with < 3 risk factors (n = 125) vs. those with > 3 risk factors (n = 95). **Results**: There were significant associations between the risk factors and the angiographic characteristics in patients with IHD. There were more significantly stenosed lesions among patients with > 3 risk factors compared to patients with < 3 risk factors ($p < 0.05$). Lesions were more diffused ($p < 0.01$), with higher incidence of left ventricular dysfunction ($p < 0.001$) among former patients compared to later ones. **Conclusions**: Significant findings were observed in the angiographic profile of patients with multiple risk factors. There were more multi-vessels and diffused angiographic findings among patients with chronic stable angina.

Keywords: *risk factor, ischemic heart disease, coronary angiography*

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1. Introduction

Coronary artery disease (CAD) due to atherosclerosis is a major cause of death all over the world and is the most common form of heart diseases. Its incidence is increasing among different populations and by 2020 it is estimated that it will be the major cause of death all over the world [1].

There is a number of personal attributes that may increase liability for development of CAD often described as risk factors. Nowadays, the prevalence of these risk factors tends to increase in developing countries compared to the developed world because of lack of institutional implementation of specific policies that target these risk factors [2].

In clinical practice coronary stenosis is often considered as the main cause of myocardial ischemia. However, other causes should be considered especially in normal coronary angoigraphy in documented cases of ischemic heart disease (IHD).

Although there are many advances in modalities for evaluation of coronary lesions, however the coronary angiography remains the "gold standard" for identifying the presence or absence of stenosis in coronary arteries and meanwhile provides reliable information during percutaneous coronary intervention [3].

The main aim of the current study is to clarify the impact of the cardiovascular risk factors on coronary angiographic profile of the Iraqi patients with IHD. Other specific objectives would rather be to test whether different coronary risk factors can influence the patterns of coronary angiography among different subtypes of IHD

presentations and to study the distribution and clustering of different cardiovascular risk factors in those patients.

2. Methods

During the period from 1st April to 31st August 2006, two -hundred twenty patients with IHD (75 females, 145 males) who aged 28-72 (mean 54.27 ± 9.1) years were enrolled in this study. They presented for the first time to Ibn-Sina Teaching Hospital in Western Mosul as STEMI (two out of three criteria; acute ischemic chest pain, ECG changes and elevated cardiac enzymes), NSTEMI &/or U.A (clinical features, ECG changes but not ST-elevation &/or elevated cardiac enzymes), and chronic stable angina(typical exertional chest pain) and underwent diagnostic coronary angiography.

The patients were categorized into three groups according to IHD presentations into STEMI (n = 72, M = 43, F = 19, mean age 53.26 ± 8.7yr), NSTEMI &/or U.A (n = 98, M = 72, F = 26, mean age 53.58 ± 9.2 yr.) and those with chronic stable effort angina (n = 50, M = 30, F = 20, mean age 55.97±9.3 yr]. Patients were then re-grouped according to number of risk factors into two groups; patients with < 3 risk factors (n = 125) vs. those with > 3 risk factors(n = 95).

The investigated cardiovascular risk factors included sex of patients, age of patients (male's age > 45 years and female's age > 55 years were considered as risk factor) [4], smoking (current active cigarette smoking), T2DM, systemic hypertension (HT), positive family history of premature CAD (any 1st degree relative of patient who had documented CAD under age of 55 years in males and under 55 years in females) [4], dyslipidemia, obesity (BMI > 30 or waist circumference > 102 cm in males and > 88cm in females), and physical inactivity where active exercise is defined as at least thirty minutes, three times weekly exercise or equivalent usual daily activities. Moderate-intensity physical activity is defined as activities that are strenuous enough to burn three to six times as much energy per minute as an individual would burn when sitting quietly, or 3 to 6 Metabolic Equivalent of Task (METs). Vigorous-intensity activities burn more than 6 METs [5].

Diabetes mellitus was diagnosed by having fasting plasma glucose (FPG) > 6.1 mmol /1 or random PG > 10.0 mmo 1/1. Known cases were included as their diagnosis was already established and were already on anti- diabetic agents. Systemic hypertension was diagnosed by having systolic blood pressure > 140 mmHg and/or diastolic one > 90 mmHg at least twice during admission&/or already diagnosed hypertensive patients on medications. Dyslipimedimia was considered if there was any abnormality in serum lipid profile {(TC > 5.25.2 mmo1/1 (20 mg/dl), (LDLC > 3.0 mmol/1 (114mg/dl), HDL-C < 0.9mmo1/1 (35mg/dl), Triglyceride > 3.2 mmo1/1 (200 mg/dl)} after 12- hours fasting.

Selective coronary angiography in multiple views along left ventriculography was performed by standard techniques after screening for renal function& hepatitis B& C viruses. CAD was considered significant when there was at least 70% reduction in the diameter of a major epicardial coronary artery (RCA, LAD, LCX) or at least 50% reduction in diameter of the left main stem artery. Angiography was considered normal when the test did not identify any obstruction of any major epicardial coronary artery. The character of the lesion was defined as diffuse by the presence of more than one significant lesion in the coronary artery or if the obstructed lesion was more than 20 mm in length.

All variables were expressed as numbers and percents or as mean± SD for continuous variables . Chi-square test was used for comparison of all variables except for mean age where ANOVA test was applied. Student's T-test was used for comparison of means. P-value less than (< 0.05) was regarded as the limit of statistical significance.

3. Results

Table 1 shows that the most common indication for angiograpgy was U.A&/or NSTEMI and that the most prevalent risk factor among all cases was male gender aged more than 45 yr. (51%) then smoking (49%) followed by HT(47.2%), dyslipidemia (40%) and NIDDM (23.5%). Smoking, gender, NIDDM, HT and dyslipidemia showed statistically significant distribution among different subgroups of patients.

Table 1. The frequencies of risk factors among subgroups of ischemic heart disease

RISK FACTORS			STEMI n (%)	NSTEMI &/ or U.A n (%)	STABLE ANGINA n (%)	Total n (%)	*p-Value
Age	Mean age ± SD		53.26±8.7	53.58±9.2	55.97±9.3	-	NS
	Male	< 45 yr.	14 (19.4)	14 (14.2)	4 (8)	32 (14)	NS
	Female	< 55 yr.	14 (19.4)	12 (12.2)	10 (20)	36 (16)	NS
Male Gender			43 (59.7)	72 (73.4)	30 (60)	145(65.9)	NS
Current Smoking			47 (65.2)	43 (43.8)	18 (36)	108 (49)	< 0.05
FamilyHx of IHD			11 (25.2)	8 (8.1)	5 (10)	24 (10.8)	NS
NIDDM			9 (12.5)	22 (22.4)	21 (42)	52 (23.5)	< 0.05
Hypertension			46 (63.8)	45 (45.9)	15 (30)	106(47.2)	< 0.05
Dyslipidaemia			18 (25)	42(42.8)	29 (58)	89 (40.0)	< 0.05
Physical Inactivity			8 (11.1)	10 (10.2)	12 (24)	30 (13.5)	NS
Obesity			9 (12.5)	12 (12.2)	13 (26)	34 (15.3)	NS

The angiographic findings were analyzed in relation to IHD subtypes and there was a higher incidence of non-significant lesions in chronic stable angina compared to acute coronary syndromes. At the same time more diffuse lesions and larger number of affected vessels were revealed in the same subtype.

The frequency of one culprit artery was higher among STEMI patients, but higher incidence of LMS lesion were encountered in U.A&/or NSTEMI. Left ventricular dysfunction was higher in acute coronary syndromes compared to chronic stable angina. Results are shown in Table 2.

Table 2. Coronary angiographic findings in relation to subtypes of IHD presentations

Angiographic characters		STEMI n (%)	NSTEMI &/or U.A n(%)	STABLE ANGINA n (%)	Total n (%)	p-Value
Vessel Disease*	N/or N.S**	13(16.1)	22(22.4)	7(14)	42(19)	< 0.05
	One V.D	38(52.8)	28(28.6)	11(22)	77(35)	< 0.001
	Two V.D	12(16.7)	25(25.5)	13(26)	50(22.7)	< 0.05
	Three V.D	9(12.5)	23(23.5)	19(38)	51(23.3)	< 0.05
Vessel Location	LMS	3 (3.3)	7 (4.7)	1 (1.0)	11 (3.2)	NS
	RCA	20 (22.4)	35 (23.8)	31 (23.9)	86 (25.9)	NS
	LAD	41 (46)	57 (38.7)	40 (42.5)	138(41.6)	NS
	LCX	25 (28.3)	48 (32.8)	22 (23.6)	95 (29.3)	< 0.01
Diffuse Lesion Character		6 (8.3)	19 (19.4)	15 (30)	40 (18.1)	< 0.05
LV Dysunction		20 (27.8)	31 (31.6)	6 (12)	57 (25.7)	< 0.05

*Numbers and percents were calculated according to total vessel lesions (1V.D + 2V.D + 3V.D) in each sub-group. Total number of stenosed lesions was 330.

** Normal &/or non-significant lesions may indicate false positive cases or lysis of thrombus in culprit vessel post period of medications or other causes like vasospastic type, arteritis.

Table 3 shows that around half of patients had clustering of > 3 risk factors (R.F). Female patients had more clustering than males ($p < 0.001$). More clustering of risk factors was noticed among U.A&/or NSTEMI. There has been a higher incidence of non- significant lesions among patients with less than 3R.F while there were higher incidences of diffuse lesions, three vessels disease, LMS lesions and LVD among patients with higher than 3 risk factors.

Table 3. Relation of risk factors clustering with patients and angiographic characteristics

Characteristics		< R. F n (%)	≥ 3 R.F n (%)	Total n (%)	p- value
Characters	Mean Age ± SD	53.50 ± 8.8	55.04 ± 9.23	-	NS
	Male gender	96 (76.8)	49 (51.8)	145 (65.8)	< 0.001
Subtypes of IHD	STEMI	47 (37.6)	25 (26.3)	72 (32.7)	< 0.05
	NSTEMI, U.A	48 (38.4)	50 (52.6)	98 (44.5)	
	Stable Angina	30 (24)	20 (21.1)	50 (22.8)	
Involved vessel	Normal/orNon-S	28 (22.4)	14 (14.7)	42 (19)	< 0.05
	One V.D	53 (42.4)	24 (25.2)	77 (35)	< 0.001
	Two V.D	26 (20.8	24 (25.2)	50 (22.7)	NS
	Three V.D	18 (14.2)	33 (34.9)	51 (23.3)	< 0.05
Left Main Stem Involvement		3 (2.4)	8 (8.4)	11 (4.9)	< 0.05
Diffused Lesion Character		13 (10.4)	26 (27.4)	39 (18)	< 0.01
LV Dysfunction		20 (16)	37 (39)	57 (25.8)	< 0.001

4. Discussion

This study was carried out to assess the effects of different factors on angiographic findings in documented cases of ischemic heart disease and to delineate the differences in the clinical, cardiovascular risk factors and angiographic characteristics of these patients. These differences may play an important role in the prevention of atherosclerotic CAD [6].

The study found a significant rate of multiple risk factors in our patients. Current smoking was highly prevalent in this study followed by HT, then dyslipidemia,

T2DM, obesity physical inactivity, and positive family history of IHD, respectively. Most of patients had risk factors in combination especially the first four risk factors i.e. smoking, HT, dyslipidemia and diabetes.

Several trials have determined the importance of controlling the risk factors especially smoking cessation and blood pressure lowering in primary and secondary prevention. However, smoking remains number one preventable cause of cardiovascular disease worldwide [7,8,9].

In males, the rate of premature onset of both STEMI & NSTEMI &/or U.A was higher than angina pectoris of premature onset & this comes in accord with Kenichi Ogawa et al. [10]. Patients with chronic stable angina in this study had higher rates of both T2DM and dyslipidemia in comparison to STEMI subgroup ($p < 0.001$). This result was similar to those offered by Gaspardone et al [11].

On the other hand, hypertension was more linked to acute coronary syndrome with significant difference compared to patients with chronic stable angina ($p < 0.05$).This is in agreement with Dunder K et al. who studied cardiovascular risk factors for stable angina versus unheralded myocardial infarction [12].

Other risk factors including positive family history of IHD, physical inactivity, obesity, gender and age of ≥ 55 years in females and ≥45 years in males showed no significant difference among subtypes of IHD presentations as was revealed by Wager and Braunwald study in 1993. They found no statistical association between these risk factors and presentations or study of IHD [13].

Collectively, the frequency of absolutely normal angiography in IHD in some studies reached up to about (13.5%), but in the current study there was a higher rate of it (19%). This is mostly due to taking near normal angiogram in consideration in this study [14,15].

In this study the frequency of totally normal and near normal angiogram was higher among acute coronary syndromes subgroups; i.e. NSTEMI&/or U.A (22.4%) and STEMI (16.1%) compared to chronic stable angina subgroup (14%) with statistically significant difference among them ($P < 0.05$). This goes with Charles et al [16]. while in Zoller et al study; (11%) of normal angiograms were found in unstable angina and this may be attributed to pure cases of unstable angina without NSTEMI in their study [17].

Although the two- vessels disease was less prevalent in STEMI (16.7%), it was more evident in chronic stable angina (26%) and NSTEMI&/or U.A (25.5%) with ($p < 0.05$). The three- vessels disease was more prevalent in chronic stable angina subgroup (38%) followed by NSTEMI&/or U.A (23.5%) and finally STEMI (12.5%) with statistically significant difference ($p < 0.05$).

These results were similar to those revealed by Cinaflone et al. who compared coronary angiographic narrowing in stable angina pectoris, unstable angina pectoris, and in acute myocardial infarction. They noticed that patients with stable angina had more narrowed arteries, more stenoses and occlusions with significant differences compared to acute myocardial infarction and unstable angina [18].

In the current study, the left main stem disease was mostly evident in cases of NSTEMI&/or U.A in-spite of lack of statistically significant differences when compared to other subgroups. This is probably due to the small sample size. In Mona et al.'s study which compared stable angina with cases of unstable angina there was no significant difference regarding involvement of left main stem artery [19].

The most common vessel involved in all subgroups was LAD (41.6%) followed by LCX(29.3%) then RCA (25.9%) and lastly LMS (3.2%) with no significant difference except in case of LCX artery involvement in which there was a significant statistical difference among subgroups ($p < 0.01$).

Similar results concerning common vessels involvement were revealed by other researchers like Shunji et al and Tewari et al [20,21]. However, on the contrary, there were no significant differences in Mona et al study regarding vessels lesion location between stable angina and unstable one.

Regarding the character of the obstructed lesion; there was more diffused lesions among chronic stable angina subgroup (30%) compared to NSTEMI&/or U.A subgroup (19.4%) and STEMI subgroup (8.3%) with statistically significant difference ($p < 0.05$). Left ventricular dysfunction (by ventriculography) was more common in NSTEMI&/or U.A subgroup (31.6%) and STEMI (27.8%) with significant difference upon comparison with stable angina subgroup (12%), $p < 0.05$. These findings go with results of Mona et al. When they noticed more LVD in cases of acute coronary syndrome, and they attributed the higher rate of LVD in unstable angina to prior myocardial infarction and ischemic attacks [19].

Of patients who had < 3 risk factors, (76.8%) of them were males and (23.2%) were females. Patients with ≥ 3 risk factors were mostly males (51.6%). There was a significant difference regarding gender distribution in the two groups ($p < 0.05$) with the rate of female sex was higher in the group of ≥ 3 R.F than in the other group. This implies that female gender in this study was more susceptible to have clustering of risk factors than males as mentioned in other references [22].

Regarding the type of IHD presentation in relation to number of risk factors, there was a statistically significant difference between patients having < 3 risk factors and those having ≥ 3risk factors in relation to IHD presentations ($p < 0.05$). This means that cases of NSTEMI&/or U.A would be more prone to have more risk factors clustering than other subgroups; probably because of the preceding history of angina. The tendency of risk factors to cluster in a patient with CAD is being increasingly recognized [23]. However as IHD can be diagnosed even in absence of conventional risk factors; meticulous researches are important to identify further hidden risk factors because "unknown" or "as yet unconfirmed" risk factors may account for up to 40% of the variation in risk of atheromatous vascular diseases [24].

The current study revealed higher incidence of normal and near normal angiograms in patients who had < 3 risk factors with significant difference when compared to results of patients with ≥ 3 risk factors. This can be explained by means of the accumulative effect of risk factors and its influence on vascular bed through different mechanisms [23].

The three vessels disease, diffused character of lesions, and left ventricle dysfunction were mostly evident in

patients having ≥ 3 risk factors. This result means that these severe angiographic characters are clearly linked to multiple & clustering risk factors. Gera S et al showed that there is a positive association of two and three vessels disease with having ≥ 3 risk factors, but in this study there was no significant difference among groups regarding two vessels disease. This could be partly related to different risk factors clusters studies in Gera S et al study [24].

The present study showed a significant relation of having multiple cardiovascular risk factors with developing more aggressive angiographic findings and it showed more diffused lesions and larger number of vessels involved in cases with chronic stable angina. It also revealed that many Iraqi patients had clusters of multiple cardiovascular risk factors and thus we recommend to implement more active polices for control of these risk factors and to conduct further comprehensive studies to determine the independent influences of individual risk factors and to investigate the role of others hidden risk factors in Iraqi patients with ischemic heart disease.

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