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Association of Major Coronary Risk Factors and Gender

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Authors' contributions

This work was carried out in collaboration between all authors. Author AS-N designed the study, wrote the protocol. Author MDM managed the literature searches, analyses of the study and author MM managed the angiograpyy process. Author SJ participated in all parts and writing the first draft of the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Aims: The aim of this study is to compare major risk factors in Coronary Artery Disease patients with significant atherosclerotic lesions in both genders.
Study Design: Cross-Sectional study.
Place and Duration of Study: From Aug 2012 to Dec 2013, 299 consecutive patients who underwent angiography at the coronary angiography laboratory in Ghaem hospital were enrolled in this study.

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Methodology: Demographic data was collected by an interviewer based on a checklist. Moreover, a member of our research group examined patients for weight, height, and blood pressure. For each patient a blood sample was taken and angiography was done by an expert. Statistical analysis was performed by SPSS version 11.5, using descriptive statistics, one-way ANOVA, and non-parametric equivalent, Kruskal- Wallis. $p<0.05$ was considered as statistically significant.
Results: Participants in this study were Iranian and 52.8% were female. The females were older than males (mean age 59±10.14 vs 58±12.4); and the majority of them were married and lived in urban areas. Among 169 patients that were recruited in the study, 95 (55.6%) had a positive history of hypertension (HTN), 77 (46.4%) hyperlipidemia, and 55 (32.5%) type 2 Diabetes Mellitus (T2DM). The observed differences in these parameters between two genders were significant ($P<0.001$, $P=0.001$ and $P=0.001$), respectively. Among the participants, 40 (46.4%) were smokers (at present or in the past).
Conclusion: Our results show that the prevalence of HLP, HTN and T2DM among Iranian women who belong to the CAD patients' population is more than men.

Keywords: Risk factors; coronary artery disease; atherosclerotic lesion.

1. INTRODUCTION

Most of the deaths and disabilities in adults worldwide is because of Atherosclerosis and it's combinations such as Coronary Artery Disease (CAD) [1,2]. Although there have been advances in treatment but still a considerable percentage of a atherosclerosis patients who are apparently healthy die suddenly without any prior symptoms [2]. This worldwide disease has several causing factors and it has established relation with smoking, Hypertension (HTN), Hyperlipidemia (HLP), and type2 Diabetes Mellitus (T2DM) [3,4]. Considering the etiology of CAD, genetic plays an important role. CAD might be affected by genetic detriments via its classic risk factors (RFs) or it might be independent of them [5]. The risk of coronary artery disease in both genders increases according to age [6]. However, in some aspects we consider gender differences. As for example before menopause, protective estrogen effects reduce the prevalence of CAD in women rather than men of the same age [6]. Comparing the major risk factors in CAD patients with significant atherosclerotic lesions in both genders is what we have studied and presented in this paper.

2. MATERIALS AND METHODS

2.1 Subjects

This cross-sectional study accompanying convenient sampling was conducted from Aug 2012 to Dec 2013. 299 consecutive patients underwent angiography at the coronary angiography lab in one of the educational hospitals in Mashhad University of Medical Sciences (Ghaem Hospital). An informed consent of participation in the study was signed by all participants. The study was approved by institutional Review Board (IRB) committee of Mashhad University of Medical Sciences (MUMS). Data was collected by an interviewer based on a checklist. Moreover, patients were examined for weight (Model: seca799l), height, and blood pressure (Omron model 116) by a member of our research group. Body Mass Index (BMI) was calculated by using the weight (kg) divided by the square of height (m^2) formula. Body weight was measured by using an analogue scale while participants only had one patient gown and height was measured by using stadiometer. The exclusion criteria were patients with non- significant lesions (defined as lumen diameter stenosis less than 50% on angiogram), congestive heart failure (ejection fraction less than 40%), surgical coronary intervention, a history of percutaneous coronary angioplasty, cerebrovascular accident, peripheral atherosclerotic disease, and a history of myocardial infarction (thrombotic events could overestimate stenosis).

According to these criteria 130 subjects were excluded. The inclusion criteria were patients with first presentation of CAD. They showed more than 50% lumen stenosis at least in one coronary artery in angiography.

2.2 Blood Sampling and Laboratory Analysis

Blood samples were collected in the morning after 15 hours fasting state just before angiography and they were sent to reference laboratory. An automated chemistry analyzer using commercially available kits was used to measure plasma glucose, serum total

cholesterol, high-density lipoprotein cholesterol, and triglyceride (TG) concentration. The serum low-density lipoprotein cholesterol concentration was calculated using Friedewald equation when the plasma TG concentrations did not exceed 398.23 mg/dL.

2.3 Angiographic Analysis

We used Judkins technique through the femoral artery for all patients who underwent a standard coronary angiography; and the angiography was performed by an experienced cardiologist.

2.4 Statistical Analysis

Statistical analysis were accomplished using SPSS version 11.5. *P*-values of <0.05 were considered as statistically significant in all the analyses. Results of categorical variables were expressed as numbers and percentages. Comparison of quantitative variables among groups was assessed by a one-way ANOVA for those with normal distribution and the ones without a normal distribution, assessing by non-parametric equivalent, Kruskal - Wallis.

2.5 Definitions

Here, in this study, the significant CAD was defined as any visible stenosis more than 50% in angiography for at least one major coronary artery or branch. Hypertension history was specified as patients' self-reported hypertension or the current use of antihypertensive medications. Hyperlipidemia was specified as self-reported history of hyperlipidemia or the use of lipid-lowering drugs. Presence of Type 2 Diabetes Mellitus was determined as participants' self- reported history of Type 2 DM or using antidiabetic drugs.

3. RESULTS AND DISCUSSION

3.1 Results

169 patients with first-time reported significant coronary artery disease participated in this study. Table 1 shows patients' demographic information. All patients were from Iran and 52.8% female. In this study men were younger than women (mean age 59 ± 10.14 *vs*.58 ± 12.4). Women mostly were married and lived in urban areas. There was no significant difference between two genders in the investigated characteristics (Table 1).

Table 2 shows clinical features of 169 patients. From169 patients enrolled in this study, 95 patients (55.6%) had a positive history of HTN, 77 patients (46.4%) HLP, and 55 patients (32.5%) T2DM. These parameters, regarding gender, showed significant difference (*P*<0.001, *P*=0.001 and *P*=0.001, respectively). However, the Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Triglyceride (TG), Total Cholesterol (Total-C), High Density Lipoprotein (HDL), Low Density Lipoprotein (LDL), and Fasting Blood Sugar (FBS) levels were not significantly different between two genders. Among the participants, 40 patients (23.7%) were smoker (past or present) and there was no significant gender differences (*P*=0.39).

Table 1. Demographic information of 169 patients with significant CAD

Parameter		Female N (%)	Male N (%)	Total N (%)	*P*-value
Gender		100(59.2)	69(40.8)	169(100)	
Race	Iranian	100(100)	69(100)	169(100)	
Marital status	Married	100(100)	66(95.7)	166(98.2)	0.48
	Single	0(0)	1(1.4)	1(0.6)	
	Urban	52(52)	28(40.6)	80(47.3)	
Lodging	Rural	32(32)	26(37.7)	58(34.3)	0.13
	Other	16(16)	15(21.7)	31(18.3)	
Age*		59.18±10.44	58.79±12.46	59.02±11.28	NS

**Reported by mean± SD*

Hypertension History (HTN.H), Hyperlipidemia History (HLP.H), Type 2 diabetes mellitus History (T2DM.H), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Triglyceride (TG), Total Cholesterol (Total-C), High Density Lipoprotein (HDL), Low Density Lipoprotein (LDL), Fasting Blood Sugar (FBS), Body Mass Index (BMI)

Table 2. Clinical features of 169 patients with significant CAD

Parameter		Female Mean ± SD	Male Mean ± SD	Total Mean ± SD	P-Value
HTN.H*		68(68)	26(37.7)	95(55.6)	<0.001
SBP(mmHg)		137.97±27.24	131.41±22.32	135.37±25.51	0.17
DBP(mmHg)		82.84±11.52	80.54±16.2	81.9±13.62	0.44
HLP.H*		56(56)	21(30.43)	77(46.4)	0.001
Lipid profile (mg/dL)	TG	158.54±67.76	150.89±63.33	155.25±65.95	0.5
	Total-c	181.48±52.57	175.9±55.09	179.3±53.47	0.51
	HDL	40.56±19.53	37.23±11.87	39.26±16.99	0.11
	LDL	119.04±41.41	109.22±39.55	115.1±40.84	0.14
T2DM.H*		42(42)	13(18.8)	55(32.5)	0.001
FBS(mg/dL)		159.2±73.55	154.22±88.65	157.09±80.05	0.37
Smoking*		26(26)	14(20.3)	40(23.7)	0.39
BMI		25.56±4.4	25.8±3.89	25.71±4.19	0.82

** Reported by N (%)*

Regarding HTN.H, one-way ANOVA of BMI yielded significant differences among groups. The means and the standard deviation has been represented in Table 3.

A test was run to evaluate the mean differences of coronary artery obstruction percentage between males and females. The mean of CAD obstruction in both men and women was 88.61 and 82.02, respectively. The observed difference was statistically significant. Obtained data shows that there is not any correlation between the number of vessels involved in CAD and gender. Furthermore, we couldn't find any gender difference in the left main (LM) involvement in CAD (Table 4).

3.2 Discussion

The common approach to the coronary artery disease and its complications (i.e. Myocardial Infarction) prevention is to control modifiable risk factors such as serum lipid levels and blood pressure [7]. CAD is two to five times more common in men than women [8,9]. So we can consider sex specific strategies to prevent CAD. This approach can be more effective for apparently healthy individuals. Based on our findings in this study, the prevalence of HLP, HTN, and T2DM among women in the Iranian CAD patient population is more than men (P=0.001, P=0.001 and P<0.001 respectively); but comparing with men, they had less lumen occupation of atherosclerotic lesions in various coronary artery territories overall (P=0.004). However, there was not any considerable difference in age and BMI between males and females were. This implies that these variables have less chance to be responsible for the gender disparities. Previous researches have demonstrated that T2DM can disturb the normal function of tunica intima layer of artery walls and increase propensity to atherosclerotic plaque evolution [10].

Studies similar to what we have done here such as Bypass Angioplasty Revascularization.

Investigation 2 Diabetes (BARI 2D) trial showed that women had less severe CAD with fewer total occlusions and higher prevalence of HTN (P<0.01) comparing with men [11]. The results of other research groups such as Pathobiological Determinants of Atherosclerosis in Youth (PADY) research group [8,12,13] and Jamee et al. [14] are similar to ours although, in some cases the measurement methods are different. However another study of CAD has produced discordant findings; in African-American population, differences in the extent of atherosclerotic lesions between men and women were less or absent [15]. Other studies showed that genetic and environmental factors are both involved in the etiology of atherosclerosis [3]; though there are racial differences in genetic predisposition to the development of coronary artery disease [16]. We can imply that some of the intra-population variabilities of genetic detriments can be reflected in race-specific gender differences in severity and the extent of atherosclerosis in coronary arteries.

Table 3. Relationship between BMI and HTN.H in all patients

BMI	Total		Female		Male	
	Mean ± SD	P-value	Mean ± SD	P-value	Mean ± SD	P-value
Positive HTN.H group	26.72±3.56		26.98±4.99		26.87±4.42	
Negative HTN.H group	24.88±3.45	**0.01**	24.4±3.54	**0.05**	24.93±3.55	**0.003**
Total	25.55±3.58		26.24±4.74		25.9±4.12	

Table 4. Information of vessel involvement in coronary angiography report of 169 patients

Parameter	Total N (%)	Female N (%)	Male N (%)	P-value
1 vessel	44(100)	19(37.5)	25(62.5)	0.27
2 vessels	45(100)	16(35.56)	29(64.44)	0.05
3 vessels	42(100)	17(40.48)	25(59.52)	0.22
More than 3 vessels	21(100)	14(66.66)	7(33.33)	0.21
LM involvement	17(100)	5(29.42)	12(70.58)	0.09

Left Main coronary artery (LM)

Another study on the Iranian CAD patients demonstrated that the prevalence of a positive history of T2DM, HLP, and HTN among women is greater than men (all *P*<0.001) [17]. Part of our findings confirm previous work by Aggarwal and coworkers [18]. They observed that women were more likely to have HLP.H, T2DM.H, and HTN.H compared to men. However, in contrast to our results, HTN.H was the only factor that showed a significant difference between men and women (*P*=0.01, OR=0.35, CI=95%) [18]. A bivariate analysis was performed by Chataut et al. [19]. and showed a statistically significant relationship between HTN and gender (*P*=0.00) Nadeem and coworkers' results demonstrated that HTN did not correlate with gender, which we disagreed with. The same results were obtained for DM and HLP [20]. However, the sample sizes from two studies were different. In addition, the difference between the study results can be attributed to the difference in the study participants (Naddem et al. recruited their participants from a coronary care unit and not from an angiography unit). The results of our study show an association between BMI and history of HTN that has been also documented by Syerreetee et al. The current study showed that BMI was correlated with HTN (P-value=0.002). However, in their study another anthropometric measurement of BMI, Waist-Hip Ratio, did not show significant correlation with BMI [21]. Similarly, other studies demonstrated that HTN correlates with BMI (*P*<0.001) [22,23].

Our research outcomes show different distribution of coronary artery disease RFs between males and females. Unfortunately because of the limitations in our study, women specific RFs such as gestational hypertension and diabetes could not be assessed. We can add some unmeasured psychosocial variables such as depression and social support to RF history in subjects. Studies showed that women encounter to more problems in these cases. Women specific and psychosocial RFs can provide a plausible basis for the result interpretation [24].

In some researches it has been demonstrated that there was lower pain threshold and lower tolerance of pain in women than men [25]. In several reports it has been suggested that, in comparison with men, women had more angina despite the less extensive lesions detected on coronary angiography [11,26]. Generally, it is probable that gender difference in patient

perception of symptoms is responsible for the different presentation of symptoms. Also, men might be less likely to show CAD symptoms than women. The reason of gender difference might be because of lagging in male patients in meeting doctors. Therefore coronary artery disease in men probably has been diagnosed in the more obstructive plaque status. Our findings of higher prevalence of CAD risk factors in the Iranian females similar to other study [27], may be because of this reason that female patients report their CAD risk factors to their doctors more than male patients.

Our results are considerable because they demonstrate that among CAD patients, women had significantly higher history of hypertension, hyperlipidemia, and type 2 diabetes. Although similar preventive strategies have been applied in men and women but our findings can propose evolution of gender specific strategies. Lifestyle modification and awareness in men needs more consideration. Further research with a larger sample size that includes other racial groups is needed to confirm our findings.

3.3 Limitation and Strength

In the present research our study design was cross-sectional, so we could not manage to consider the cause and effect relationship between variables. Based on the study exclusion criteria, 130 patients were excluded from the study and this has reduced the sample size to 169 patients. It is likely that larger sample size would produce different results.

There was not significant inconsistency in the angiography studies because all the angiographies were performed by one interventional cardiologist. Our response rate was 100%. According to exclusion criteria all analysis was performed on new cases of CAD that have reduced the risk of biased selection.

4. CONCLUSION

Our results demonstrated that hypertension, hyperlipidemia, and type 2 diabetes mellitus are major risk factors for significant CAD in Iranian population, especially in women. Also the results of our study can be used to improve Iranian lifestyle. The results of our study can be served to develop preventing CAD strategies among Iranian women.

ETHICAL APPROVAL

This study was approved by Mashhad University of Medical Sciences ethical board. An informed consent was obtained from all the participants.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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