Risk Factors Associated with Coronary Artery Disease in Gaza

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Keywords: low density lipoprotein, high density lipoprotein, serum cholesterol, coronary artery disease.

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RISKFACTORSASSOCIATEDWITHCORONARYARTERYDISEASEINGAZA

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Conclusion: the means of cholesterol, TG, LDL and HDL were low and close to international ranges, while, the distribution of Sedentary Physical Activity of females, male smokers and the stressed females were the highest risk factors. All of those results are depend on genetic factors, life style and nutrition in our area. In addition, we noticed the total cholesterol/HDL ratio is most effective CAD indicator.

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I. Introduction

CAD has been remaining the first killer and the major cause of public health problems in the world, which is one of the most common causes of morbidity and mortality in different communities (Hadii et al., 2016). however, CAD is the main cause of death in the United States of America among human adults representing approximately one-third of all dead people, who are over the age of 35 yrs. (Hadaegh et al., 2009). CAD develops through narrowing of the coronary arteries which leads to death of portion of the heart muscle because of lacking of blood flow that supply

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oxygen and nutrition, and leads to heart attack (Fakhrzadeh al., 2008). Which is depend on different factors. CAD development and progression is stimulated by environmental and/or genetic factors. The environmental factors include tobacco use, diabetes mellitus (DM), and hypertension (Hadii et al., 2016). In most cases, CAD has a multifactorial genetic basis, involving a number of genes and environmental factors, which are interacting to determine whether or not the disease will develop as well as its severity (Hadii et al., 2016). Several biochemical processes participating in CAD development, include lipid and apolipoprotein metabolism, inflammatory response, endothelial function, platelets function, thrombosis, fibrinolysis, and blood pressure regulation (Marenal., 2008). Lipid blood profile plays the essential role of lipid deposition in artery wall and CAD development, by accumulating the LDL inside layers of artery wall, except HDL which has beneficial effects for a number of reasons by decreasing lipid oxidation after depositing in blood vessels, leading to retarding CAD development. In other observational studies were shown that each 1-mg/dL decrease in plasma HDL concentration is associated with a 2% to 3% increased risk of CAD (Chapman et al., 2004). So, HDL is called "good cholesterol" according to its beneficial role in blood vessels by many mechanisms to prevent LDL from depositing on blood arteries, in contrast LDL is called "bad cholesterol" due to its role.

II. Coronary Artery Disease Risk Factors

a) Uncontrollable CAD risk Factors

Age: Is among the most important risk factors for predicting incident cardiovascular disease. Based on previous experience studies in the United States the average risk of developing cardiovascular disease for a 30-34 year old male is 3%, this number raises some sevenfold to 21% for a comparable individual aged 60–64 years (Wilson et al., 1998). The exact importance of age-related risk compared with other cardiovascular disease risk factors illustrated by the Framingham Heart Study that has resulted in a 14-point scoring system to predict incident 10-year cardiovascular disease. In this system, the increasing risk characterized by a higher score, up to 7 points can be attributed to age alone (Stocker et al., 2004). According on a previous Research, that suggests that 80–90% of patients with

CAD have at least 1 of the 4 modifiable risk factors (DM, hypertension, hypercholesterolemia and smoking) **(Canto et al., 2011)**.

Gender or sex; is important risk factor in incidence of CAD and many studies noted difference between male and female in CAD distribution among population **(Canto et al., 2011)**.

b) Controllable CAD risk factors

The body mass index: Is a key index measurement for relating a person's body weight to their height. It had been used by the World Health Organization (WHO) as the standard for recording obesity statistics since the early 1980s **(Eknoyan., 2008)**.

Obesity or overweight: Is defined as an excess in body weight with an abnormal high preponderance of body fat. The obesity has become a major public health issue in the United States **(Bibbins et al., 2007)** and the prevalence of obesity in the developed world is increasing at an alarming rate **(Stocker et al., 2004)**. In addition, obesity leads to other metabolic disorders and constitutes a major cardiovascular risk. however, in fact, 50% to 66% of the world population is obese **(Balkau et al., 2007)**.

Stress: Is the way of metabolic body reacts to change, includes our mental, emotional, and physical responses to the pressures of everyday life, with change is a natural and normal part of life, therefore a moderate amount of stress is part of normal living **(Health Library., 2009)**. Stress may be good by acting body motivate and more productive, while the strong stress response is a harmful with set the body for general poor health as well as specific psychological or physical illnesses like heart disease or infection.

Hypertension: Is defined as a systolic blood pressure in excess of 140 *mmHg* or a diastolic blood pressure above 90 mmHg **(Pressure., 1993)**. Uncontrolled high blood pressure can result in hardening and thickening of the coronary arteries, narrowing the channel through which blood can flow. In observation study it was referred that the hypertension was considerably more frequent among cases than control subjects. Therefore, the hypertension considers the main risk factor of CAD development in many populations **(Hopkins et al., 2005)**.
- Diabetes Mellitus (DM): is defined as an increased of blood glucose level (hyperglycemia). Recent and previous studies observed the presence of a strong association between CAD development and DM, therefore the DM is consider one of the main risk factor of CAD development **(Nishigaki et al., 1981)**.

Cigarette: Smoking could promote atherosclerosis, in part, by its effects on lipid profile. Smokers have significantly higher serum cholesterol, triglyceride, and LDL levels, but HDL is lowering in smokers than in nonsmokers **(Ambrose et al., 2003)**. It was estimated that the smoking increases atherosclerotic disease by 50% and doubles the incidence of CAD **(Al-Refaee and Al-Hazzaa., 2001)**. The nicotine constricts blood vessels, and carbon monoxide (CO) can damage their inner lining, making them more susceptible to atherosclerosis. However in both animal and human models, several studies have demonstrated that the cigarette smoking exposure were associated with a decrease in vasodilatory function **(Ambrose et al., 2003)**.

Physical activity: The regular exercise or physical activities consider the most important and the beneficial treatment methods for people that under CAD risk **(Al-Refaee and Al-Hazzaa., 2001)**. In the United States of America (USA) an epidemiological research on physical activity revealed that the physical inactivity appears to be a more important CAD risk factor **(Al-Refaee and Al-Hazzaa., 2001)**.

To the best of our knowledge, this is the one of the first studies in Gaza strip investigating the significance of the association of lipid profile and other risk factors with CAD development in Gaza population.

III. Method and Sample

a) Target Population

In this cross-sectional of population survey study, fresh blood samples of 94 CAD patients were collected from cardiology department of central hospital "El shefaa" of Palestinian Ministry Health – Gaza strip. In addition the period of samples collection started from 1/6/2008 to 16/8/2008.

The first confirmed diagnosis of CAD patients such as (Ischemic Heart Disease, Myocardial Infraction and Angina) was detected via cardiology department physicians.

Fresh blood samples were obtained from the fast hospitalized CAD patients and asymptomatic Patients without prior history of CAD or taking medications to control CAD risk factors, then it were analyzed by automatic spectrophotometer for serum cholesterol, serum TG, LDL and HDL.

b) Questionnaire

Other requested data were collected via questionnaire in English language. Data were collected using the standard interview method with physician of cardiology department, stuff nursing and patients. The main questions were about personal history of hypertension, dyslipidemia, DM and CAD, smoking, use of smokeless tobacco and alcohol, diet. Questions concerning income, education and physical activity, stress, Body Mass Index (BMI) were included. Questions related to history of documented prior myocardial infarction (MI), unstable angina, coronary artery bypass graft (CABG) surgery, noninvasive investigations for CAD, coronary angiography, coronary angioplasty, documented use of drugs for CAD and hospital admission for CAD.

c) Analysis

All obtained data from questionnaire blood lipid profile values, HDL/LDL ratio, LDL/HDL ratio and total cholesterol/HDL ratio were entered and analyzed in Self-Propelled Semi-Submersible (SPSS) version 15 software, the following tests were applied: Frequency and distribution, Student T-test and Chi square test.

d) Ethical considerations

The approval letter for the present study was obtained from the Helsinki committee at the Palestinian Ministry of Health (MOH). n addition, all the subjects involved in the present study signed a formal consent form about their agreement to be involved in the present study. All parts of the present study were performed in accordance with the Helsinki Declaration of 1975.

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IV. RESULTS

The sample size of the current study was 94 CAD Palestinian patients in Gaza strip, which included 68 (72.3%) males and 26 (27.7%) females. The mean of CAD patients age was (57.3±12.8 yrs), the mean age of males was (56.0±13.2 yrs) and for females it was (60.5±11.1 yrs), among three age groups (≤45 yrs), (46-65 yrs) and (≥66 yrs).

We noticed the distribution of CAD patients at higher risk were the middle age group **(P<0.001)**. As shown in table-2 the mean of body weight was (83.0±12.3kg) and the mean of body height was (28.7±6.070 Cm), so the mean of females Body Mass Index (BMI) was higher than males with significant difference **(P=0.001)**, while, the Overweigh females group were higher than males group with significant difference **(P=0.001)**.
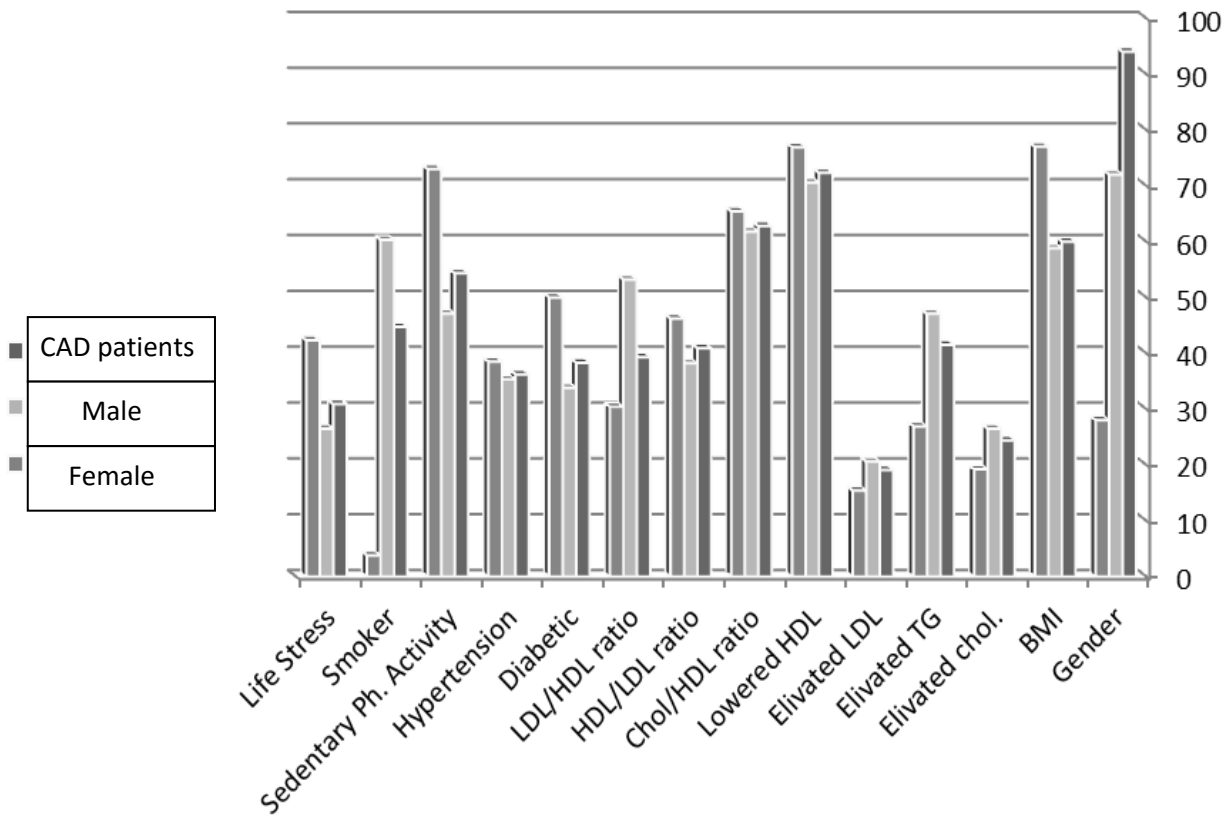

Figure 1: The distribution of CAD patients with CADF risk factors

Table 1: The average of risk factors and comparison in Palestinian (Gaza strip) CAD patients

Risk factor	Total (Mean +SD)	Male (Mean +SD)	Female (Mean +SD)	P-value (T-test)
BMI (kg/m^2)	(28.7±6.0)	(27.4±4.0)	(31.9±8.8)	**P=0.001**
serum cholesterol (<200mg/dl)	(167.3±62.2)	(166.0±57.7)	(170.8±73.9)	P > 0.05
serum TG (>150mg/dl)	(163.7±82.5)	(170.4±85.2)	(146.3±73.7)	P > 0.05
serum LDL (>160mg/dl)	(99.7±59.8)	(96.6±51.5)	(107.9±78.4)	P > 0.05
serum HDL (<40 mg/dl)	(34.8±12.5)	(35.3±13)	(33.6±11.2)	P > 0.05
Total cholesterol to HDL ratio (>4:1)	(5.3±2.8)	(5.0±1.9)	(5.9±4.3)	P > 0.05
HDL to LDL ratio (<0.3)	(0.5±0.4)	(0.5±0.4)	(0.4±0.3)	P > 0.05
LDL to HDL ratio (3.2)	(3.2±2.6)	(2.9±1.7)	(3.9±4.2)	P > 0.05
The significant difference is < 0.05 level.				

The means of males hypercholesterolemia and hypertriglyceridemia were statistically higher than females (**P<0.008**).

In other side, the Sedentary Physical Activity was observed an elevated in our CAD patients, moreover, the mean of females was higher than males with significant difference (as shown in table 2). The male Smokers were higher than females with no significant difference with regard (**P=0.302**). By contrast, the stressed females group were higher than males with significant difference (**P=0.001**). Moreover, during analyzed data we noticed the ratio of Total cholesterol/HDL (**62.8%**) was the most indicator than HDL/LDL (40.3%) and LDL/HDL ratio (39.3%).

Table 2: The number of distribution of CAD patients with CADF risk factors

CAD risk factor	Patients	Male	Female	P-value (chi square)
• Gender	100%	72%	28%	(P=0.001)
- (≥66year) group	22.3%	17.6%	34.6%	(P < 0.05)
- (46-65year) group	58.5%	60.3%*	53.8%	(P < 0.001)
- (≤45year) group	19.1%	22.1%	11.6%	(P < 0.05)
• BMI (Obese and Overweight)	60%*	58.8%	77%	(P = 0.003)
- Overweigh group	31.0%	25%	46.2%*	(P<0.001)
- Obese group	33.0%	33.8%	30.8%	(P < 0.05)
- normal weight group	36.0%	41.2%*	23.1%	(P = 0.003)
• Elevated cholesterol (>200mg/dl)	24.4%	26.5%	19.2%	(P < 0.05)
- high cholesterol level group (>240mg/dl)	17%	19.1%	11.5%*	(P < 0.008)
- the borderline level group (<240 – >200mg/dl)	7.4%	7.4%	7.7%	(P < 0.05)
- normal level group (<200mg/dl)	75%	73.5%	80.8%	(P < 0.05)
• Elevated TG (>150mg/dl)	41.5%	47.1%	26.9%	(P < 0.05)
- high level group (>200mg/dl)	23.4%	26.5%	15.4%	(P < 0.05)
- borderline level group (<200 – >150mg/dl)	18.1%	20.6%	11.5%	(P < 0.05)
- normal level group (<150mg/dl)	58.5%	52.9%	73.1%	(P < 0.05)
• Elevated LDL (>160mg/dl)	19.1%	20.6%	15.4%	(P < 0.05)
- high level (undesirable) group (>160mg/dl)	19.1%	20.6%	15.4%	(P < 0.05)
- normal level group (<160mg/dl)	80.9%	79.5%	84.6%	(P < 0.05)
• Lowered HDL (<40mg/dl)	72.3%	70.6%	76.9%	(P < 0.05)
- very high level group (>60mg/dl)	6.4%	8.80%	3.9%	(P < 0.05)
- high level group (<60 – >40mg/dl)	21.3%	20.6%	19.2%	(P < 0.05)
- low level (undesirable) group (<40mg/dl)	72.3%	70.6%	76.9%	(P < 0.05)
• Total chol/HDL ratio	--	--	--	--
- high ratio group (>4:1)	62.8%*	61.8%	65.4%	(P > 0.05)
- safe ratio group (<4:3.5)	13.8%	14.7%	11.5%	(P < 0.05)
- ideal ratio group (<3.5)	23%	23.5%	23.1%	(P < 0.05)
• HDL/LDL ratio	--	--	--	--
- high risk ratio group (0-0.9)	40.9%	38.2%	46.2%	(P > 0.05)
- moderate risk ratio group (0.9-0.14)	1.1%	0.0%	3.8%	(P > 0.05)
- average risk ratio group (0.14-0.22)	2.1%	1.5%	3.8%	(P > 0.05)
- low ratio group (0.22-0.30)	20.2%	20.6%	19.2%	(P > 0.05)
- normal ratio group (>0.30)	59.6%	61.8%	53.8%	(P > 0.05)

• LDL/HDL ratio		--	--	(P > 0.05)
- high risk ratio group (0-0.9)		4.0%	0.0%	(P > 0.05)
- moderate risk ratio group (0.9-0.14)		4.1%	1.4%	(P > 0.05)
- average risk ratio group (0.14-0.22)		20.0%	12.0%	(P > 0.05)
- low ratio group (0.22-0.30)		25.0%	17%	(P > 0.05)
- normal ratio group (>0.30)		46.8%	69.7%	(P > 0.05)
				(P > 0.05)
• Diabetic		33.8%	50%*	(P = 0.02)
• Hypertension		35.3%	38.5%	(P =0.723)
• Sedentary Ph. Activity		47.1%	73%	(P=0.001)
• Smoker		60.3%	3.8%	(P =0.302)
• Life Stress		26.5%	42.3%*	(P =0.001)

= The significant relation (is < 0.05 level).

In the current study the reference values for optimal and high levels of blood lipids profile were based on the world studies as follows; the National Cholesterol Education Program (NCEP) used the optimal serum cholesterol level <200 mg/dL, serum TG level <160 mg/dL, serum HDL level >40 mg/dL for both sexes and serum LDL optimal level was <100 mg/dL.

As shown in table-1 and 2, the mean age of CAD patients (57±12 yrs), and the mean age of female patients was (60±11 yrs). In addition we observed that the total mean of elevated BMI risk factor was (28.7±60 kg/m^2).

• *Lipid profile:* In our study, the percentage of cholesterol in males have a higher level of cholesterol than females (P=0.008).

The distribution of the TG in our study as risk factor was 41.5% (47.1% males and 26.9% females), in addition, it was found that the TG males are higher than TG females.

The distribution of low serum HDL as risk factor was 72.3% (70.6% males and 76.9% females), in current study we noticed that the mean of serum HDL females was lower than males.

In the current study, it was found that the mean of serum LDL was (99.7±59.8 mg/dl) while the mean of males was higher than females. In addition, the distribution of serum LDL level (≥161mg/dl) is 19.1% (20.6% males and 15.4% females). Therefore, the males distribution is higher than females.

• *Other risk factors:*

- The distribution of sedentary physical activity among females was significantly higher than their male counterparts (P= 0.001).
- In addition it was found the distribution of cigarettes smokers as a risk factor was 44.7% (60.3% males and 3.8% females).

Also the distribution of females life stressed CAD patients as risk factor was the third highest factor. The means of males hypercholesterolemia and hypertriglyceridemia were statistically higher than females (P<0.008).

In other side, the Sedentary Physical Activity was observed an elevated in our CAD patients, moreover, the mean of females was higher than males with significant difference (as shown in table 2). The male Smokers were higher than females with no significant difference with regard (P=0.302). By contrast, the stressed females group were higher than males with significant difference (P=0.001). Moreover, during analyzed data we noticed the ratio of Total cholesterol/HDL (62.8%) was the most indicator than HDL/LDL (40.3%) and LDL/HDL ratio (39.3%).

In the current study the reference values for optimal and high levels of blood lipids profile were based on the world studies as follows; the National Cholesterol Education Program (NCEP) used the optimal serum cholesterol level <200 mg/dL, serum TG level <160 mg/dL, serum HDL level >40 mg/dL for both sexes and serum LDL optimal level was <100 mg/dL.

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V. Discussion

In the current study the reference values for optimal and high levels of blood lipids profile were based on the world studies as follows; the National Cholesterol Education Program (NCEP) used the optimal serum cholesterol level <200 mg/dL, serum TG level <160 mg/dL, serum HDL level >40 mg/dL for both sexes and serum LDL optimal level was <100 mg/dL. The same values were used in regional studies such as; in Jordan (Hammoudeh et al., 2008), Islamic Republic of Iran (Qazvin) (Fakhrzadeh al., 2008), Islamic Republic of Iran (Tehran) (Hadaeghet al., 2009) and Palestinian (Jerusalem) and Jewish women (Jabara et al., 2007).

As shown in table-1 and 2, the mean age of CAD patients is similar to population of Iran as described in Tehran study. And the mean age of female patients is closed to population of Palestinian and Jewish women study (Jabara et al., 2007). So our study agreed with the result of those study (Fakhrzadeh al., 2008).

In the current study, we observed that the total mean of elevated BMI risk factor is closed to population of Iran and Jordanian, as described in Tehran study (Hadaegh et al., 2009), Qazvin study (Fakhrzadeh al., 2008) and Jordan study (Hammoudeh et al., 2008). Which is due to similarity of the demographic differences among the population as shown in various studies emphasize the fact that each society has its own demographic characteristics and social behavior, which is reflected on the overall findings of each study.

So we recommended to use the risky borderline >45mg/dl rather than >40mg/dl for female in our population, as recommended in Jordanian study (Hammoudeh et al., 2008).

- *Lipid profile:* In our study, we found that the average of cholesterol is the lowest of all the regional studies, while the percentage of cholesterol in males have a higher level of cholesterol than females, this agreed with Kuwaiti study, which found that the fasting level of hypertriglyceridemia more prevalent than hypercholesterolemia among Kuwaiti population and reported that the previous hypothesis of hypertriglyceridemia is an important risk factor for CAD patients in Kuwait (Olusi et al., 2003). While this does not agree with Tehran study (Hadaegh et al., 2009) and Jordanian study (Hammoudeh et al., 2008).

In addition, the distribution of the TG in our study as risk factor is less than populations of Qazvin study (Fakhrzadeh al., 2008) And Jordan study (Hammoudeh et al., 2008). Moreover, it was found that the TG males are higher than TG females, which is agree with Qazvin study (Fakhrzadeh al., 2008), and the mean of serum TG is nearly similar to that of Jordan study (Hammoudeh et al., 2008).

The distribution of low serum HDL as risk factor is higher than Qazvin study (Fakhrzadeh al., 2008), and in Jordan study (Hammoudeh et al., 2008) and Tehran study (Hadaegh et al., 2009). In addition, in current study we noticed that the mean of serum HDL females was lower than males, but higher than Jordanian study (Hammoudeh et al., 2008) and Tehran study (Hadaegh et al., 2009), while, in Jordanian study the author referred to the mean of low HDL was significantly lower in females CAD patients (Hammoudeh et al., 2008), but it does not agree with the Qazvin study. Moreover, in Qazvin study the author referred to the prevalence of CAD in African–American patients with low HDL level (Fakhrzadeh al., 2008). So we recommended to use the risky borderline >45mg/dl rather than >40mg/dl for female in our population, as recommended in Jordanian study (Hammoudeh et al., 2008).

In the current study, it was found that the mean of serum LDL is less Jordan study (Hammoudeh et al., 2008), while the mean of males was higher than females, which agreed with Jordanian study (Hammoudeh et al., 2008). In our study the distribution of serum LDL level (≥161mg/dl) is closed to Qazvin study. While, the males distribution is higher than females, which doesn't agree with Qazvin study (Fakhrzadeh al., 2008). By comparing lifestyle and socioeconomic of Gaza population with Kuwait population, it was noticed that the level of LDL in healthy population was higher and the author referred that It seems likely that diet may be an important contributory factor to high LDL mean and distribution as cholesterol mean, particularly the saturated fatty acids, which those with 12 to 16 carbon atoms and increases LDL-cholesterol. Also, the author referred that the Kuwaitis eat a lot of saturated fatty acids from meat and cholesterol from eggs, dairy products and sweets and this may partly explain their high serum total cholesterol concentrations (Olusi et al., 2003).

In another study, it was referred that the diet of economically underdeveloped populations contain low total calories, saturated fat, and cholesterol (Rao et al., 1980), but our population has different lifestyle and socioeconomic situation. Therefore, we noticed the LDL mean and distribution were low. So, we recommend applying the new cut off >70mg/dl of LDL level, particularly in Cardiovascular Disease (CVD) patients, Diabetic and CAD patients under risk. The total cholesterol/HDL ratio is considered a good indicator for CAD prognosis and monitor. In general, lipid profile is determined mainly by the quality and quantity of food whether it is fat-rich or low-fat diet. This affects the lipid blood levels. Each society has its own food habits other risk factors should be taken into consideration as well. These facts may explain-in part, the differences between our study and other studies.

- *Other risk factors:*

- The distribution of sedentary physical activity among females was significantly higher than their male counterparts (P= 0.001), which agreed with Tehran study (Hadaegh et al., 2009). Also, in Tehran study the author referred that the women has lower levels of physical activity than men in general. Moreover, our result agreed with Arabic and Jewish study (Jabara et al., 2007), where the author reported that the Arabic women Jerusalem has less physical activity exercise, while the higher physical active population is protected by exercise, more than physical light and moderate populations (Jabara et al., 2007). Therefore, we suggested the same speculation in our population.

  In our culture, females feel shy when they perform physical activity, for this reason the majority of females do not conduct activity at regular basis, in addition, many of the females in our society remain at their homes for long periods.

- In addition it was found the distribution of cigarettes smokers as a risk factor is higher than populations of Jordanian study (Hammoudeh et al., 2008), Jewish women, Palestinian women (Jabara et al., 2007) and Qazvin study (Fakhrzadeh al., 2008), but less than Tehran study (Hadaegh et al., 2009).

  Also the distribution of females life stressed CAD patients as risk factor was high, which agree with Arabic and Jewish study (Jabara et al., 2007). Therefore, we have suggested that the same condition is present in our population, especially the population of Gaza who are suffering from low socioeconomic and other conditions and this causes stress to population. Also, in Arabic and Jewish study, however, the author referred that the Palestinian women has less education and lower socioeconomic status than Jewish women. In addition, the Palestinian women patients were younger and had more children than Jewish women (Jabara et al., 2007), and the socioeconomic status particularly in women has consistently been associated with increased cardiovascular morbidity and mortality (Jabara et al., 2007). It was reported in other study, The psychosocial stress and lifestyle factors are related to most of increased risk factors (Hadii et al., 2016). In addition, other research suggests that the co-existence of biological and lifestyle/behavioral risk factors is highly prevalent in disadvantaged and underserved populations with low socioeconomic status (Everage et al., 2014).

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