



## Impact of Diabetes Mellitus on Coronary Artery Disease in Women Attending Coronary Angiography in Gaza- Palestine: An Observational Study

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### Authors' contributions

This work was carried out in collaboration between all authors. Authors AJ and YA designed the study, wrote the protocol and completed analysis. Author AJ completed the data entry wrote the first draft of the manuscript and managed the literature searches. Authors GN, MR, KER and MH completed data collection. All authors read and approved the final manuscript.

### Article Information

DOI: 10.9734/CA/2015/17940

Editor(s):

(1) Luca Masotti, Internal Medicine, Cecina Hospital, Italy and Post-graduate School in Geriatrics, University of Siena, Italy.

Reviewers:

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(4) Anonymous, University of A Coruña, Spain.

Complete Peer review History: <http://www.sciencedomain.org/review-history.php?iid=1198&id=26&aid=9242>

Original Research Article

Received 30<sup>th</sup> March 2015

Accepted 21<sup>st</sup> April 2015

Published 14<sup>th</sup> May 2015

### ABSTRACT

**Aims:** It is well known that Diabetes Mellitus (DM) is a crucial risk factor for Coronary artery disease (CAD). The present study aimed to investigate characteristics and angiographic profiles of the CAD in diabetic women in comparison with non-diabetics.

**Methodology:** Documented CAD was examined in 688 women, attending angiographic examination in El-Hayat cardiology center in Gaza City during the period 2010 – 2013. Cross-sectional design was applied in this study where variables of interest are examined at the same point of the women examination, and predisposing risk factors were recorded. CAD severity was assessed by the number of arteries 0-3 with more than 50% stenosis.

**Results:** 420 of the study population (61%) were diabetics, the diabetic women were older ( $P = 0.02$ ), had higher prevalence of hypertension, high level of Systolic blood pressure (SBP) and Diastolic

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blood pressure (DBP) and high level of Triglycerides (TG), the P value for all these variables cited was less than 0.001. The Body mass index (BMI) was the same in the two groups ( $P=0.76$ ); women with diabetes have higher prevalence of severe stenosis in the angiography, where normal vessel was reported in 36.4%, single vessel 26.9%, double vessels 18.6% and triple vessels 18.1% vs 57.8%, 17.9%, 12.7%, 11.6% in non diabetic's women respectively with significant statistical difference ( $P=0.001$ ). Binary logistic regression analysis showed that diabetes mellitus was stronger predictor of CAD.

**Conclusion:** Our data shows a strong association of diabetes effect more than other factors, on atherosclerosis. Information for future prospective studies is needed for primary, secondary and tertiary prevention of cardiovascular disease in Palestine.

*Keywords: Diabetes mellitus; coronary angiography; women; Gaza-Palestine.*

## 1. INTRODUCTION

Diabetes affect around 100 million population worldwide [1] and the prevalence of diabetes for all age group was found to be 2.8% in 2000, 6.4% in 2010 and estimated to be 7.7% in 2030 [2]. CAD is the most leading cause of mortality of female in most developed countries [3-4]. Limited data are available on CAD among women in Palestine. In a study found in Gaza-Palestine 2015 about risk factors among women with CAD showed that diabetes is 2 times higher in women with CAD compared with normal coronaries [5].

The association between diabetes and Coronary events in women is more powerful for women than men [6]. DM was one of the most important risk factor for the development of CAD recently considered as a CAD risk equivalent [7]. Furthermore, women with diabetes have a greater than 3-fold increase in CAD risk than non diabetics [8] and higher mortality 3-5 times in women compared with the general population [9]. The relative risk of myocardial infarction was 50 percent greater in diabetic male and by 150 percent greater in diabetic's women [10]; diabetic's women have more than 40% greater risk of incident compared with diabetics male. The Framingham study and other studies showed 2-to 4 fold higher prevalence of CAD in diabetics compared to non diabetic with high risk of mortality in diabetic's women [11-14]. Numerous studies conducted in American and European population have shows that rates for CAD events are equivalent to both individuals with CAD and diabetic subjects without CAD [15], [13-17]. In addition the presence of diabetes increased the risk for CAD in both premenopausal and post menopausal women [18], in the nurse health study each year of earlier menopause increased coronary risk by 2% to 3% [19]. On the other hand CAD is considered as one of the most important

complication of diabetes in all type of diabetes and in both sexes [20].

The objective of this study was to examine what diabetics patients differ from non-diabetic patients in terms of patient's characteristics and angiographic findings.

## 2. METHODOLOGY

This is an observational study based on the records of 688 women attending angiographic examination in El-Hayat cardiology center in Gaza City. 420 were diabetics and 268 were non diabetics. Cross sectional Variables available in the records for the years 2010 - 2013 are recorded in abstract sheet. Cross sectional design is applied in this study where variables of interest are examined at the same point of the women examination. All diabetic patients were already on insulin or anti diabetics agents, according to the information provided by the patients, the non diabetics were considered as a control group. Preliminary evaluation of all patients included clinical characteristics as, age, residence, Hypertension, family history of coronary artery disease, systolic and diastolic blood pressure, lipids profiles, fasting blood glucose, hemoglobin and clearance creatinine level were tested. Clearance creatinine is calculated according to Cockcroft-Gault equation  $(140 - \text{age}) \times \text{weight (kg)} / 72 \times \text{serum creatinine (mg/dl)}$  multiply by 0.85 for women [21]. The degree of obesity was expressed as BMI calculated by Quetelets formula  $(\text{weight (kg)} / \text{high(m}^2))$  [22] and According to National Institutes of Health (NIH) and WHO guidelines values between  $18.5 - 24.9 \text{ kg/m}^2$  are normal weight, 25 and  $29.9 \text{ kg/m}^2$  are considered overweight and greater than  $30 \text{ kg/m}^2$  are obese. Resting electrocardiogram and echocardiography to asses left ventricular function (LV) was

performed for all study population. The severity of CAD was assessed by the number of arteries 0,1,2,3 with more than 50% reduction of luminal diameter of the coronary artery in angiography. The number of affected vessels was recorded and confirmed by two cardiologists, [23] and angiography was considered as normal when the test did not identify any major lesion in epicardial artery. We included all cases presented to the center to perform coronary angiography for the first time therefore we excluded all patients with history of prior cardiac surgery, percutaneous coronary intervention and valvular heart disease.

The ethical committee (Helsinki) in Gaza approved this study. Finally Data management and analyze were performed using statistical package SPSS software version 20. Simple frequencies, means and standard deviation for continuous variables were calculated. Student's t test and chi square test were used to compare values between the two groups of diabetics and non diabetics. Logistic regression analysis was performed to control for confounders. Statistical significance is measured by OR and the confidence interval. P value less than 0.05 was considered as significant.

### 3. RESULTS

Our study results reveal differences between 420 diabetics and 268 non diabetic patients attending a private cardiac angiography center located in Gaza city. Table (1) shows higher percentage of the study population lives in Gaza city and the diabetics in the city were (63.3%) and the non diabetics (36.7%). Differences in diabetes in the different localities are not statistically significant. The majority of our study population is in age group 53 years and more (81.2%), therefore (64.4%) of them were diabetics. Since diabetics are older menopause percentage is higher among diabetics than non diabetics (63.5% vs. 36.5%) respectively and the differences are statistically significant ( $P = 0.002$ ). Obesity is known risk factor for both diabetes mellitus and coronary artery disease. Thus percentage of obesity was higher in diabetics (62.5%) than non diabetics (37.5%) but the differences are not statistically significant. Diabetics have higher percentage of hypertension (68.6%) than non diabetics (66.0%) and the differences in hypertension percentage among the two groups reach statistical significant level ( $P < 0.001$ ). The

family history of CAD in study population is (27.0%) and it is more prevalent in diabetics (55.9%) without statistical significant differences. In brief diabetics were older with higher percentage of menopause and hypertension.

Table (2) presents the clinical and laboratory characteristics of the study population. The mean age of diabetics is 61.63 years and for non diabetics is 60.25 years, despite that age differences are not statistically significant and we are intending to include age in logistic regression analysis to adjust for age differences. In addition our findings demonstrate differences with statistical significant level between diabetics and non diabetics, in both systolic and diastolic blood pressure, the same trend is observed for cholesterol and triglycerides where much higher levels are reported among diabetics. Little differences were observed in hemoglobin concentration and clearance creatinine between the two groups.

To continue the summary of our estimation we conclude in Table (3) that the prevalence of coronary artery disease among the study population was (55.2%) and when we compare diabetics and non diabetics for diagnosis findings including electrocardiogram (ECG), echocardiography and coronary angiography findings. we observed that among (56.4%) of diabetics patients often present with acute coronary syndrome (ACS) include (STEMI, NSTEMI, unstable angina) or stable angina in opposite not diabetics have others symptoms (41.4%) like dyspnea, palpitation or atypical chest discomfort, the difference between two groups in clinical status was statically significant ( $P= 0.001$ ), also diabetics subject have 2.4 times to develops ACS than no diabetics. Abnormal ECG findings are reported in (64.3%) of diabetics and (61.9%) of non diabetics and the difference is not statistically significant. Also diabetics patients had more depressed myocardial function as compared with non diabetics patients, left ventricular function ( $EF < 55$ ) was observed in (58.1%) among diabetics compared with (52.2%) among the non diabetics without statistical significant differences. Coronary angiography findings show marked statistically significant differences in coronary disease between the two groups where diabetics are (63.6%) and non diabetics are (42.2%), ( $P < 0.001$ ) with risk of 2.4.

**Table 1. Baseline characteristics of study population with and without diabetes**

	Diabetic N=420		Not diabetic N=268		Total N=688		OR (95%CI)	P value
	NO	%	NO	%	NO	%		
<b>Residence</b>								
North	79	54.9	65	45.1	144	20.9	1	0.21
Gaza city	236	63.3	137	36.7	373	54.2	1.4(0.9-2.0)	0.08
South	105	61.4	66	38.6	171	24.9	1.3(0.8-2.1)	0.24
<b>Age group</b>								
32y-52y	60	46.5	69	53.5	129	18.8	2.1(1.4-3.1)	0.002
53y and more	360	64.4	199	35.6	559	81.2		0.29
<b>Body mass index</b>								
Normal (18.5-24.9kg/m <sup>2</sup> )	10	58.8	7	41.2	17	2.5	1	0.75
Overweight(BMI25-29.9 kg/m <sup>2</sup> )	64	54.7	53	45.3	117	17	0.8(0.3-2.3)	0.76
Obese (BMI>30 kg/m <sup>2</sup> )	346	62.5	208	37.5	554	80.5	1.2(0.4-3.1)	
<b>Hypertension</b>								
Yes	386	68.6	177	66	563	81.8	5.8(3.7-8.9)	0.001
NO	34	27.2	91	72.8	125	18.2		
<b>Menopause</b>								
Yes	372	63.5	214	36.5	586	85.2	1.9(1.2-2.9)	0.002
NO	48	47.1	54	52.9	102	14.8		
<b>Family history of CAD</b>								
Yes	104	55.9	82	44.1	186	27	1.3(0.9-1.9)	0.09
NO	316	62.9	186	37.1	502	73		

**Table 2. Clinical and laboratory characteristic of study population, comparison of the means between two groups**

Variable	Diabetic	Not diabetic	P value
Mean age	61.63	60.25	0.077
SBP (mmhg)	148.3±19.4	139.8±19.9	0.001
DPB (mmhg)	83.3±9.9	80.7±9.8	0.001
Hemoglobin (g/dl)	11.7±1.2	11.8±1.3	0.161
Cholesterol (mg/dl)	196.4±49	184.1±47.5	0.051
Triglyceride (mg/dl)	232.8±116	170.7±82	0.001
FBS (mg/dl)	190.9±65.2	109.4±33.1	0.001
Clearance creat (mg/dl)	96.6±47.6	104.1±54.8	0.591

**Table 3. Clinical and functional indices in both groups**

	Diabetic N=420		Not diabetic N=268		Total N=688		OR (95%CI)	P value
	NO	%	NO	%	NO	%		
<b>Diagnosis</b>								
ACS	237	56.4	108	40.3	345	50.1	2.4(1.7-3.4)	0.001
Stable angina	83	19.8	49	18.3	132	19.2	1.9(1.2-2.9)	0.005
Atypical chest pain	100	23.8	111	41.4	211	30.7	1	0.001
<b>Electrocardiogram</b>								
normal	150	35.7	102	38.1	252	36.6	1.1(0.8-1.5)	0.533
abnormal	270	64.3	166	61.9	436	63.4		
<b>Left ventricular function</b>							1.2(0.9-1.7)	
EF<55	244	58.1	140	52.2	384	55.8		0.131
EF≥55	176	41.9	128	47.8	304	44.2		
<b>Coronary angiography</b>							2.4(1.7-3.2)	
Normal coronaries	153	36.4	155	57.8	308	44.8		0.001
Coronary disease	267	63.6	113	42.2	380	55.2		

The angiographic feature for the two groups are demonstrated in Table (4) as the regards the severity of CAD, in the two age group the non diabetics patients had one vessel disease less than the non diabetic (17.9% vs 26.9%), ( $P=0.006$ ). With no serious difference, in age group less than 53 years. Two vessel diseases in age group 32-53 years was ten times higher in diabetic than non diabetics, while in age group 53 years and more two vessel disease was more in diabetics group with approximately double risk. However three vessels disease was more frequent in diabetic's patient with a risk of eight times more in age group 32-53 years, also we noted the increasing results of CAD with increasing age in diabetics patients rising from (23.3%, 11.7%, 8.3%) to (27.5%, 19.7%, 19.7%) respectively for one, two, three vessels disease. In addition normal coronary was more present in young diabetic than older diabetic women (56.7%, 33.1%) respectively and the same observation was noted in non diabetics women (79.7%, 50.3%).

Results of logistic regression analysis in our study demonstrate that CAD is the disease of

older women, the disease increase as age increase, so history family, hypertension and diabetes are working independent on the development of CAD women (Table 5).

#### 4. DISCUSSION

As one of the major risk factors, diabetes is associated with higher morbidity and mortality of CAD [8]. Most guidelines consider diabetes as a cardiovascular equivalent and a poor prognosis factors in ACS. In 2002 the national cholesterol education program report designated diabetes as CAD equivalent, the report explain that intensive prevention strategy is justified in diabetics patients because of their high risk new CAD within 10 years [24]. Epidemiological data from the Framingham study demonstrated a 2-4 fold increase in atherosclerosis disease in diabetics' patients and the risk of death from Cardiovascular disease for patients with diabetes compared to patients without DM [25]. Also the new recommendation by the American Diabetic Association (ADA) and American heart association (AHA) consider that diabetes be consider a coronary artery disease equivalent

**Table 4. Difference between both groups with respect to the number of normal arteries and arteries with lesion higher than 50% in different age group**

Age group		Diabetic N=420		Not diabetic N=268		OR (95%CI)	P value
		NO	%	NO	%		
32-53 years	No vessels disease	34	56.7	55	79.7	1	0.001
	One vessel	14	23.3	12	17.4	1.9(0.7-4.6)	0.154
	Two vessel	7	11.7	1	1.4	11.3(1.3-96)	0.007
	Three vessel	5	8.3	1	1.4	8.0(0.9-72)	0.029
53 years and more	No vessels disease	119	33.1	100	50.3	1	
	One vessel	99	27.5	36	18.1	2.3(1.4-3.7)	0.000
	Two vessel	71	19.7	33	16.6	1.8(1.1-2.9)	0.02
	Three vessel	71	19.7	30	15.1	1.9(1.2-3.3)	0.01
Total population	No vessels disease	153	36.4	155	57.8	1	0.001
	One vessel	113	26.9	48	17.9	2.4(1.5-3.5)	0.006
	Two vessel	78	18.6	34	12.7	2.3(1.5-3.7)	0.000
	Three vessel	76	18.1	31	11.6	2.5(1.5-4.0)	0.000

**Table 5. Logistic regression analysis with coronary artery disease as dependent variable and other risk factors as independent variables**

	B	SE	P. value	OR (95%CI)
Age group	1.148	0.215	0.000	2.1-4.8
Hypertension	0.462	0.186	0.013	0.4-0.9
Family history of CAD	0.382	0.221	0.085	0.4-1.1
Diabetes mellitus	0.723	0.174	0.000	0.3-0.7
constant	0.813	0.450	0.071	

rattan than a risk factor [26-27]. Most studies performed in diabetics' patients with ACS showed that the atherosclerosis is severe and more diffuse. Diabetes is a metabolic disorder that affects micro and macro vasculature lead to metabolic and endothelial change, and increase the platelets aggregation, consequently increase the risk of rupture of the plaque and thrombus formation [28-29].

Coronary angiography remains the Gold standard technique for identifying and evaluating CAD [30]. This study showed the characteristic and angiographic finding in diabetics women than non diabetic, our results demonstrated that Diabetics were slightly older than non diabetics with a mean age of 61.6 years and statistical significance difference was found between the two groups, concerning age group, BP, percentage of HTN, level of triglyceride and cholesterol in opposite minor difference for other variables as level of hemoglobin, clearance creatinine. For a Percentage of positive FHCAD, this relation could be explaining by the association, between diabetes and family history, where Cicone MM et al. found that family history of diabetes increase cardiovascular risk [31,32]. And we noted that obesity was remarkable among two group, in addition coronary insufficiency symptoms was more important in diabetics patients, the same results was found in a study done in 2014 in India shows that ACS in women was 32% in diabetics vs. 20% in non diabetics with more severe coronaries lesions [33] and another similar study done in Iraq in 2011 which showed that diabetic patients were more likely to have involvement more vessels than non diabetics [34] and there was no difference in age between two group. Observation from de VALLIANT trial and the OASIS registry demonstrated that diabetics Patients have a higher prevalence of HTN, Hyperlipedemia with more severe symptom compared to non diabetics patients and patients presenting with ACS Had worse long term outcome compared to non diabetics [35-36].

In the present study difference in characteristics of CAD between patient with and without DM were detected by Coronary angiography, a significant positive correlation between the presence of DM and number of vessel was demonstrated, (44.8%) of general population have normal coronaries and (55.2%) had CAD however more severe angiographic findings was found in diabetic than in non diabetics (63.6%)

vs. (42.2%) respectively this results was equivalent to a study conducted in AFIC-NIHD Rawalpindi (India) published in 1999 showed that (35.6%) of females were found to have normal coronaries and (64.4%) had coronary artery disease with a mean age of 53 years [37], likewise a study done in 2006 in Pakistan included 100 females 8% had diabetes and 27% had combined diabetes and hypertension all diabetics females had CAD while patients with both HTN and DM 85% had CAD [38]. However menopausal women (age group 53 and more) had more significant artery (three vessel diseases), than younger women (age group 32-53) (19.7%) vs. (8.3%). Our data was counterpart with a study done in 2008 in Athens, Greece. and a review article by Hani holy 2014 conclude that diabetic menopausal women develop more severe CAD compared to non diabetes and triple the risk for CAD, so diabetes eliminates the protective effect of female gender [39,40]. In addition diabetes was associated with impaired of systolic function, the prevalence of EF<50% in diabetics women was significant (58.1%) this is due to specific changes that occur including diabetic autonomic neuropathy, diabetic cardiomyopathy and silent ischemia which impaired myocardial performance render the myocardium more susceptible and less able to recover from ischemia [41,42]. This is coming on line with a study done by Jose Marconi et al in 2004 in Brazil performed among 645 women undergoing coronary angiography the diabetics group was older, higher prevalence of post menopausal and had more severe 3 vessels disease and low EF<50% [43]. The major limitation of this study is the lack of access to follow-up the patients and the data is based only on the available records.

## 5. CONCLUSION

Our study shows that increasing age, with diabetes, and Hypertension are the most significant strong risk factors for CAD in Palestinian women and suggest an independent effect of diabetes on atherosclerosis process. This study aims at providing baseline information for future prospective studies, and health care services are needed for primary, secondary and tertiary prevention of cardiovascular disease.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

The ethical committee (Helsinki) in Gaza approved this study. The study is record based and all names are excluded (Anonymous). Authors did not interview any patient. All results presented for groups and presented by percentages.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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