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ORIGINAL RESEARCH

Risk Factors for Coronary Heart Disease Among Lebanese Women: A Case–Control Study

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Purpose: Women are increasingly concerned by coronary heart disease (CHD), with peculiarities of their own, particularly concerning risk factors. The aim of the study was to assess the risk factors for CHD in Lebanese women over forty.

Patients and Methods: A case–control study was carried out in 6 hospitals in Beirut and Mount-Lebanon, from December 2018 to December 2019 including 1500 patients (1200 controls and 300 cases). Women were stratified into pre- and post-menopausal groups. Personal and medical data were collected from hospital records and during an interview where validated questionnaires were used. Binary logistic regressions were performed to investigate potential predictors of CHD in the 2 groups.

Results: In post-menopausal women, dyslipidemia (adjusted odds ratio [aOR], 3.018; 95% confidence interval, 2.102–4.332), hypertension (aOR: 2.449, [1.386–4.327]), a family history of CHD (aOR: 2.724, [1.949–3.808]), cigarette smoking (aOR: 2.317, [1.574–3.410]) and common non-rheumatic joint pain (aOR: 1.457, [1.053–2.016]) were strongly associated with CHD. Conversely, living in Mount Lebanon seemed protective, compared to Beirut (aOR: 0.589, [0.406–0.854]), as well as having a moderate monthly income (aOR: 0.450, [0.220–0.923]), adhering to a Mediterranean diet (aOR: 0.965, [0.936–0.994]), and practicing physical activity [PA] (aOR: 0.396, [0.206–0.759] and 0.725, [0.529–0.992], respectively for high and moderate vs low PA). In pre-menopausal women, dyslipidemia (aOR: 6.938, [1.835–26.224]), hypertension (aOR: 6.195, [1.318–29.119]), family histories of dyslipidemia (aOR: 6.143, [1.560–24.191]) and CHD (aOR: 4.739, [1.336–16.805]) reached statistical significance.

Conclusion: The identification of factors associated with CHD in women, some of which are frequent and trivialized in post-menopause, underlines the need to put in place specific and dedicated CHD prevention strategies in women.

Keywords: coronary disease, risk factors, aging, pre-menopausal women, post-menopausal women

Introduction

According to recent world health organization (WHO) data, coronary heart disease (CHD) remains the leading cause of death worldwide, with increasing prevalence in Africa and Middle East countries,[1] and ranked as the main cause of death in Lebanon.[2] While premenopausal women have a lower cardiovascular risk than men, it is well recognized that their risk catches up to that of men as they age and change their hormonal status.[3] Also, recent epidemiological studies show a more important decrease in CHD mortality rates in men compared to women.[4]

Although everyone shares most traditional risk factors (RFs), a significantly different gender weighting seems to exist. Some RFs might have a higher impact on women's cardiovascular disease (CVD) risk. Women are also increasingly adopting smoking and alcohol consumption.[5] Moreover, environmental stressors caused by urban living or urbanization (population density, economic activity, transportation, sanitation, long-term exposures to air pollution, noise, lack of surrounding greenery, building morphology, ….) cannot be denied as factors leading to cardiovascular health problems, especially among women.[6,7]

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This relation was also demonstrated by previous work, indicating the effect of living in Beirut, the capital of Lebanon, on heart disease compared with outside of Beirut; where older participants and women were more likely to report cardiovascular risk factors (CVRFs) than younger participants and men.[8,9] Furthermore, it has been reported that the medical management of women, due to various factors (failure to consider initial symptoms, delay in medical consultation, sometimes less pathognomonic symptomatology) could differ significantly from that of men, increasing the risk of medical problems.[10] Thus, despite women living longer than men, many of those extra years are spent in poor health.[11]

Some studies have previously been interested in CVRFs in the general Lebanese population[12,13] due to the considerable impact of the topic in public health and the need to improve knowledge of a medical problem which appears to be worsening.[9] However, women are under-represented in heart disease research (about 20% of enrolled patients in most clinical studies),[10] while CVD accounting for one third of all female deaths.[14] This lack is not in accordance with the health, social and environmental evolution of society. The aim of our study is to carry out an analysis of the RFs for CHD in Lebanese women over 40, based on a case-control study. This would allow us to develop avenues of reflection to propose an improvement in the medical prevention of these women who are currently less concerned with cardiovascular risk programs.

Materials and Methods

Study Design and Study Population

A case-control study was carried out in Beirut and Mount-Lebanon, approved by the Institutional Review Board ethical committee of each participating hospital, in accordance with Lebanon's ethical legislation, and the Declaration of Helsinki. Six hospitals were contacted to obtain their authorization to participate in the study (Central Military Hospital, Lebanese Hospital Geitaoui, Sacred Heart Hospital, Makassed General Hospital, Mount-Lebanon University Hospital, and Rafik Hariri University Hospital). Eligible patients were selected from hospital admission lists and their informed consent was obtained prior to enrollment.

Women aged over 40, hospitalized between December 2018 and December 2019, without previous heart disease (myocardial infarction [MI], CHD, valvular heart disease, cardiomyopathy, and myocarditis) could be included. The cases group was composed of women diagnosed with CHD (MI, or stable/unstable angina) for the first time, and control group consisted of women randomly selected from surgery and general medicine departments of the same hospitals with no personal history of CHD.

Cancer, mental disorder, human immunodeficiency virus, end-stage renal disease, chronic steroid treatment and pregnancy were exclusion criteria.

Data Collection

Data were obtained from medical records and questionnaires completed during a face-to-face interview after assessing participants' capacity to respond using the Abbreviated Mental Test Score.[15]

The data collected, secondarily anonymized, were: socio-demographics (age, marital status, educational level, working status, monthly income and place of residence (Beirut, Mount-Lebanon, South Lebanon and Nabatieh, North Lebanon and Bekaa Valley)), lifestyle data (smoking, eating habits (using Lebanese Mediterranean Diet Score (LMDS)[13]), alcohol consumption and self-reported pollution exposure (closeness to generators, traffic, factories, …)[16]). Joint pain, rheumatic diseases, periodontitis, and post-menopausal status were self-declared. Medical and family histories were evaluated, in relation to the onset of premature CHD, presence of CVRFs and comorbidities. Several health-related scores such as medication adherence (Lebanese Medication Adherence Scale (LMAS),[17] Beirut Distress Scale-22 (BDS-22),[18] physical activity (PA, International Physical Activity Questionnaire (IPAQ)),[19] and sedentary lifestyle were calculated.

Sample Size

Sample size was calculated using Epi info7, assuming a Type I error of 5%, a study power of 80%, and a confidence interval (CI) of 95%. We used the CHD prevalence (9% in over forty Lebanese women[13]) in our calculation. Thus, the minimum sample size necessary to show a double increase in CHD risk, in a ratio case/control of 1/4, was 1500 participants.

Individual RFs Definitions

Hypertensive women were either self-declared, taking anti-hypertensive drugs or with a hospitalized blood pressure measured over 140/90 mmHg. Women with diabetes were defined as taking hypoglycemic drugs, self-declared or those with biological evidence for diabetes (blood sugar: fasting ≥7 mmol/L or random ≥11.1 mmol/L or glycated hemoglobin ≥6.5%). Dyslipidemia was defined through self-reporting, lipid-lowering treatment, or by biological data when available (non-High-Density Lipoprotein Cholesterol (non-HDLc) ≥3.4 mmol/L; triglycerides ≥1.7 mmol/L; or Low-Density Lipoprotein Cholesterol (LDLc) ≥3 mmol/L).

A family history of premature CHD was defined as a first-degree relative who developed CHD before the age of 55 for men and 65 for women.

Body Mass Index (BMI) was calculated (overweight defined as BMI ≥25 kg/m^2 and obese as BMI ≥30 kg/m^2). Menopause was considered to be present when there was no history of menstruation for 12 consecutive months.

Environmental and Behavioral RFs Definitions

Income per family member was defined as the monthly household income of the family divided by the number of its members, and categorized into low, middle or high income according to the poverty line and the minimum wage adopted in Lebanon.[20]

Exposure to outdoor (living area, closeness to a road, traffic jam, an electricity generator, or factories and exposure to gases or toxic substances) and indoor (heating and cooking methods) air pollution[16] was also assessed based on patients' self-reported information.

The women's residence was further analyzed in terms of CHD RFs, highlighting the impact of living in the Lebanese capital (Beirut) compared to outside Beirut.

Women who had smoked cigarettes and/or waterpipes in the previous 12 months were considered current smokers and those who had quit smoking more than a year earlier were considered former smokers. The cumulative doses of cigarettes and waterpipes were computed as the average number of daily packs or weekly waterpipes respectively, multiplied by the duration of smoking.[21] Exposure to secondhand smoking (home or workplace) was defined by the self-declared average exposure period in daily hours from the previous week.[22]

The IPAQ long form assessed the level of PA in four domains: work, domestic, transport and leisure; PA intensity was evaluated by frequency (days/week) and duration (min/day) over the past 7 days.[23] The total volume of PA was computed by weighting each type of activity by its estimated energy needs (metabolic equivalent (MET): 3.3 for walking, 4 for moderate PA and 8 for vigorous PA) generating a combined score in MET.minutes/week (low amount: <600, moderate: 600 to <3000 and high PA levels ≥3000 MET.min/week). We have also estimated sedentary periods, for weekdays and weekends.

Dietary habits were evaluated using LMDS, consisting of twenty major components, distributed into 10 beneficial and 10 harmful foods.[13] Scores varied from 0 to 80 (maximal adherence to Mediterranean diet).

Psychological distress was measured using BDS-22,[18] composed of 22 questions and reflecting 6 factors (depression, demotivation, psychosomatic, mood deterioration, intellectual inhibition and anxiety), with a Likert scale (0-never to 3-always). Possible scores range from 0 to 66 (maximum psychological distress).

Patient Medication Adherence was assessed by the LMAS composed of occupational, psychological, annoyance and economic factors.[17] The sum of all items vary from 0 to 14 (maximum therapeutic adherence).

Statistical Analysis

Data were analyzed using SPSS, version 21. Descriptive statistics including percentages and means (± standard deviations) were used to describe patients' characteristics. Bivariate analyses were performed using Student's *t*-test to verify the association between CHD and continuous variables, or with the adjusted *t*-test. For categorical variables, Pearson-Chi^2 and Fisher exact tests were used to compare percentages. Crude odds ratios (OR) and adjusted OR with their respective 95% CI were reported. The reliability of some scores was estimated by calculating Cronbach's alpha (>0.7: acceptable). The candidate predictors for the multivariate analyses were identified by taking those which had

a p-value <0.20 in the bivariate analysis. Two multivariate logistic regression models (using the "backward" method) were performed to control for confounding variables (particularly age) and determine independent predictors of CHD among pre- and post-menopausal women. A p-value <0.05 was considered significant. The final models were reached after ensuring the adequacy of data using Hosmer-Lemeshow test, and the absence of any multicollinearity between predictors using the correlation matrix.[24]

Results

Sample Description and Sociodemographic Patients' Characteristics

From 2146 women initially screened, 646 (30.1%) were not included, leading to a study size of 1500 patients (1200 as controls (80%) and 300 as cases (20%)) (Figure 1).

Women were divided into pre- and post-menopausal groups. Table 1 shows the baseline socio-demographic characteristics of the study sample. CHD patients were significantly older in both groups (46.44±4.27 vs 44.48±3.82 in pre-menopausal group, and 66.68±9.38 vs 65.39±10.73 in post-menopausal group, for cases and controls, respectively). Almost half (48.7%) of the non-coronary post-menopausal women lived in Mount-Lebanon, while 28% of cases lived in the capital Beirut.

Lifestyle and Individual RFs for CHD

As expected, usual RFs of CHD emerged in our study (Table 2). Regarding risky behaviors, current cigarette smoking was associated with CHD in pre-menopausal (OR: 4.878 [1.441–16.508]) and post-menopausal (OR: 1.917 [1.431–2.567]) women, where a clear positive dose-response relationship between pack-years and odds of CHD was also demonstrated. Moreover, the majority of individual RFs were significantly and markedly more common in CHD patients of both groups.

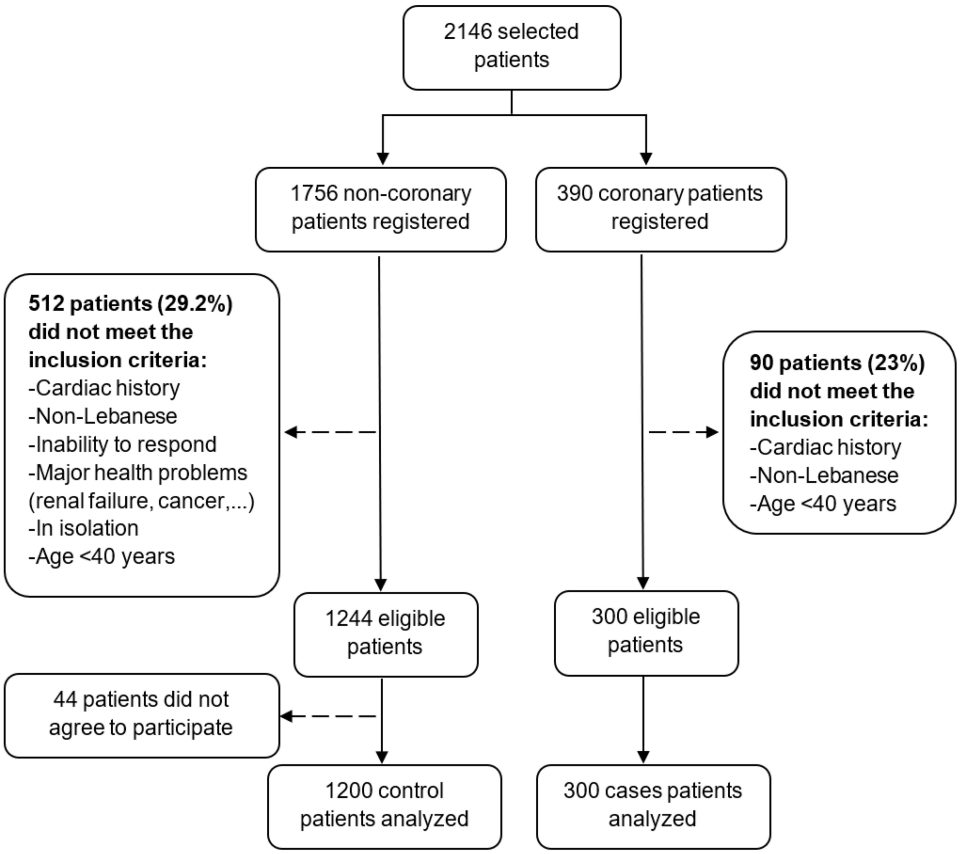

Figure 1 Flowchart of women included in the study.

Table 1 Baseline Socio-Demographic Characteristics of Study Population

Characteristics	Pre-Menopausal Women n (%) 192 (12.8%)			Post-Menopausal Women n (%) 1308 (87.2%)		
Total Patients: 1500	**Controls 174 (90.6%)**	**Cases 18 (9.4%)**	**P-value**	**Controls 1026 (78.4%)**	**Cases 282 (21.6%)**	**P-value**
Age (years)	44.48 ± 3.82	46.44 ± 4.27	0.047*	65.39 ± 10.73	66.68 ± 9.38	0.049*
Place of residence			0.297			0.020*
Beirut	36 (20.7%)	5 (27.8%)		231 (22.5%)	79 (28.0%)	
Mount Lebanon	79 (45.4%)	6 (33.3%)		500 (48.7%)	108 (38.3%)	
South Lebanon/Nabatieh	12 (6.9%)	1 (5.6%)		77 (7.5%)	21 (7.4%)	
North/ Akkar	21 (12.1%)	5 (27.8%)		121 (11.8%)	36 (12.8%)	
Bekaa/Baalback/Hermel	26 (14.9%)	1 (5.6%)		97 (9.5%)	38 (13.5%)	
Type of living area			0.576			0.238
Urban	45 (25.9%)	6 (33.3%)		301 (29.3%)	93 (33.0%)	
Rural/peri-urban	129 (74.1%)	12 (66.7%)		725 (70.7%)	189 (67.0%)	
Marital status			0.221			0.118
Married	135 (77.6%)	17 (94.4%)		540 (52.6%)	132 (46.8%)	
Divorced/widowed	16 (9.2%)	1 (5.6%)		432 (42.1%)	138 (48.9%)	
Single	23 (13.2%)	0		54 (5.3%)	12 (4.3%)	
Working status			0.784			0.489
In professional activity	49 (28.2%)	4 (22.2%)		74 (7.2%)	17 (6.0%)	
Unemployed/ Retired	125 (71.8%)	14 (77.8%)		952 (92.8%)	265 (94.0%)	
Educational level			0.198			0.115
Illiterate/or primary school level	23 (13.2%)	5 (27.8%)		418 (40.7%)	137 (48.6%)	
Complementary school level	59 (33.9%)	4 (22.2%)		386 (37.6%)	96 (34.0%)	
Secondary school level	40 (23.0%)	6 (33.3%)		125 (12.2%)	28 (9.9%)	
University	52 (29.9%)	3 (16.7%)		97 (9.5%)	21 (7.4%)	
Monthly income of the women's family			0.582			0.143
< 500,000 LBP	11 (6.3%)	1 (5.6%)		214 (20.9%)	56 (19.9%)	
500,000–1,000,000 LBP	22 (12.6%)	1 (5.6%)		195 (19.0%)	54 (19.1%)	
1,000,000–2,000,000 LBP	83 (47.7%)	7 (38.9%)		373 (36.4%)	106 (37.6%)	
2,000,000–4,000,0000 LBP	53 (30.5%)	9 (50.0%)		202 (19.7%)	63 (22.3%)	
> 4,000,000 LBP	5 (2.9%)	0		42 (4.1%)	3 (1.1%)	
Monthly income per individual			0.608			0.129
Low (<180,000 LBP/month/person)	14 (8.0%)	1 (5.6%)		33 (3.2%)	16 (5.7%)	
Middle (180,000–675,000 LBP/month/person)	120 (69.0%)	11 (61.1%)		732 (71.3%)	191 (67.7%)	
High (>675,000 LBP/month/person)	40 (23.0%)	6 (33.3%)		261 (25.4%)	75 (26.6%)	

Notes: Data are presented as count (%). *P <0.05 was considered significant.
Abbreviation: LBP, Lebanese pounds.

We also found that common joint pain, was significantly associated with higher odds of CHD (OR: 2.985 [1.020–8.734] and 1.686 [1.270–2.237] for pre- and post-menopausal groups, respectively).

Environmental and Behavioral RFs for CHD

Our results (Table 3) showed that a toxic respiratory environment is associated with CHD in women with a significant result for passive smoking (OR: 4.541 [1.011–20.393] and 1.401 [1.075–1.828] for pre- and post-menopausal women, respectively), while declared exposure to pollution tended to be higher among cases, but did not reach statistical significance.

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Table 2 Differences in Lifestyle and Individual Risk Factors According to Studied Women Status

Characteristics	Pre-Menopausal Women n (%) 192 (12.8%)				Post-Menopausal Women n (%) 1308 (87.2%)			
	Controls 174 (90.6%)	Cases 18 (9.4%)	OR (95% CI)	P-value	Controls 1026 (78.4%)	Cases 282 (21.6%)	OR (95% CI)	P-value
BMI (mean ± SD)	29.32 ± 6.67	29.53 ± 5.40	1.005 (0.934–1.081)	0.896	29.70 ± 6.68	29.62 ± 5.86	0.998 (0.978–1.019)	0.868
Smoking status (cigarette/or waterpipe)								
Non-smoker	80 (46.0%)	4 (22.2%)	1.00 (Ref.)	–	542 (52.8%)	112 (39.7%)	1.00 (Ref.)	–
Active smoking history	2 (1.1%)	0	–	0.999	77 (7.5%)	20 (7.1%)	1.257 (0.738–2.140)	0.400
Current active smoker	92 (52.9%)	14 (77.8%)	3.043 (0.963–9.620)	0.058	407 (39.7%)	150 (53.2%)	1.784 (1.353–2.352)	<0.001*
Previous smoking status								
Never	80 (46.0%)	4 (22.2%)	1.00 (Ref.)	–	542 (52.8%)	112 (39.7%)	1.00 (Ref.)	–
Cigarette	0	0	–	–	55 (5.4%)	15 (5.3%)	1.320 (0.720–2.419)	0.370
Waterpipe	3 (1.7%)	0	–	0.999	26 (2.5%)	2 (0.7%)	1.936 (1.445–2.593)	<0.001*
Mixed smoking	0	0	–	–	6 (0.6%)	4 (1.4%)	1.452 (0.393–5.360)	0.576
Current smoking status								
Never	80 (46.0%)	4 (22.2%)	1.00 (Ref.)	–	542 (52.8%)	112 (39.7%)	1.00 (Ref.)	–
Cigarette	41 (23.6%)	10 (55.6%)	4.878 (1.441–16.508)	0.011*	308 (30.0%)	122 (43.3%)	1.917 (1.431–2.567)	<0.001*
Waterpipe	48 (27.6%)	3 (16.7%)	1.250 (0.268–5.826)	0.776	89 (8.7%)	25 (8.9%)	1.359 (0.834–2.215)	0.218
Mixed smoking	3 (1.7%)	1 (5.6%)	6.667 (0.561–79.287)	0.133	10 (1.0%)	3 (1.1%)	1.452 (0.393–5.360)	0.576
Total cigarette smoking, quantification (for previous and current smokers)								
Non smoker	130 (74.7%)	7 (38.9%)	1.00 (Ref.)	–	647 (63.1%)	138 (48.9%)	1.00 (Ref.)	–
Up to 20 pack-years	23 (13.2%)	4 (22.2%)	3.230 (0.875–11.923)	0.078	125 (12.2%)	28 (9.9%)	1.050 (0.670–1.646)	0.831
More than 20 up to 40 pack-years	16 (9.2%)	2 (11.1%)	2.321 (0.444–12.149)	0.319	122 (11.9%)	44 (15.6%)	1.691 (1.144–2.499)	0.008*
More than 40 pack-years	5 (2.9%)	5 (27.8%)	18.571 (4.338–79.511)	<0.001*	132 (12.9%)	72 (25.5%)	2.557 (1.819–3.596)	<0.001*
Total waterpipe smoking, quantification (for previous and current smokers)								
Non smoker	120 (69.0%)	14 (77.8%)	1.00 (Ref.)	–	895 (87.2%)	248 (87.9%)	1.00 (Ref.)	
Up to 30 waterpipes-years	16 (9.2%)	2 (11.1%)	1.071 (0.223–5.154)	0.931	25 (2.4%)	3 (1.1%)	0.433 (0.130–1.446)	0.174
More than 30 waterpipes-years	38 (21.8%)	2 (11.1%)	0.451 (0.098–2.075)	0.307	106 (10.3%)	31 (11.0%)	1.055 (0.691–1.613)	0.803
Hypertension								
No	122 (70.1%)	3 (16.7%)	1.00 (Ref.)	–	257 (25.0%)	23 (8.2%)	1.00 (Ref.)	–
Yes	52 (29.9%)	15 (83.3%)	11.731 (3.257–42.250)	<0.001*	769 (75.0%)	259 (91.8%)	3.763 (2.402–5.898)	<0.001*
Diabetes								
No	147 (84.5%)	11 (61.1%)	1.00 (Ref.)	–	615 (59.9%)	127 (45.0%)	1.00 (Ref.)	–
Yes	27 (15.5%)	7 (38.9%)	3.465 (1.234–9.731)	0.018*	411 (40.1%)	155 (55.0%)	1.826 (1.400–2.382)	<0.001*
Dyslipidemia								
No	136 (78.2%)	4 (22.2%)	1.00 (Ref.)	–	480 (46.8%)	62 (22.0%)	1.00 (Ref.)	–
Yes	38 (21.8%)	14 (77.8%)	12.526 (3.896–40.277)	<0.001*	546 (53.2%)	220 (78.0%)	3.119 (2.294–4.242)	<0.001*
Declared joint pain								
No	93 (53.4%)	5 (27.8%)	1.00 (Ref.)	–	432 (42.1%)	85 (30.1%)	1.00 (Ref.)	–
Yes	81 (46.6%)	13 (72.2%)	2.985 (1.020–8.734)	0.046*	594 (57.9%)	197 (69.9%)	1.686 (1.270–2.237)	<0.001*

Rheumatic diseases								
No	170 (97.7%)	18 (100.0%)	1.00 (Ref.)	–	972 (94.7%)	270 (95.7%)	1.00 (Ref.)	–
Yes	4 (2.3%)	0	–	0.999	54 (5.3%)	12 (4.3%)	0.800 (0.422–1.517)	0.494
Periodontitis								
No	144 (82.8%)	14 (77.8%)	1.00 (Ref.)	–	841 (82.0%)	223 (79.1%)	1.00 (Ref.)	–
Yes	30 (17.2%)	4 (22.2%)	1.371 (0.422–4.458)	0.599	185 (18.0%)	59 (20.9%)	1.203 (0.866–1.670)	0.270
Family history of								
- Premature CHD								
No	142 (81.6%)	7 (38.9%)	1.00 (Ref.)	–	861 (83.9%)	184 (65.2%)	1.00 (Ref.)	–
Yes	32 (18.4%)	11 (61.1%)	6.973 (2.509–19.383)	<0.001*	165 (16.1%)	98 (34.8%)	2.779 (2.066–3.738)	<0.001*
- Stroke								
No	173 (99.4%)	18 (100.0%)	1.00 (Ref.)	–	1016 (99.0%)	277 (98.2%)	1.00 (Ref.)	–
Yes	1 (0.6%)	0	–	1.00	10 (1.0%)	5 (1.8%)	1.834 (0.622–5.410)	0.272
- Hypertension								
No	103 (59.2%)	8 (44.4%)	1.00 (Ref.)	–	624 (60.8%)	152 (53.9%)	1.00 (Ref.)	–
Yes	71 (40.8%)	10 (55.6%)	1.813 (0.682–4.820)	0.233	402 (39.2%)	130 (46.1%)	1.328 (1.018–1.731)	0.037*
- Diabetes								
No	98 (56.3%)	9 (50.0%)	1.00 (Ref.)	–	627 (61.1%)	167 (59.2%)	1.00 (Ref.)	–
Yes	76 (43.7%)	9 (50.0%)	1.289 (0.488–3.406)	0.608	399 (38.9%)	115 (40.8%)	1.082 (0.827–1.416)	0.565
- Dyslipidemia								
No	153 (87.9%)	10 (55.6%)	1.00 (Ref.)	–	936 (91.2%)	254 (90.1%)	1.00 (Ref.)	–
Yes	21 (12.1%)	8 (44.4%)	5.829 (2.069–16.417)	0.001*	90 (8.8%)	28 (9.9%)	1.146 (0.734–1.791)	0.548

Notes: Data are presented as count (%) or mean ± standard deviation (SD). *P <0.05 was considered significant.
Abbreviations: OR, odds ratio; CI, confidence interval; BMI, body mass index; CHD, coronary heart disease.

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Table 3 Difference in Various Environmental and Behavioral Risk Factors According to Studied Women Status

Scores	Cronbach's Alpha	Pre-Menopausal Women n (%)				Post-Menopausal Women n (%)			
		192 (12.8%)				1308 (87.2%)			
		Controls 174 (90.6%)	Cases 18 (9.4%)	OR (95% CI)	P-value	Controls 1026 (78.4%)	Cases 282 (21.6%)	OR (95% CI)	P-value
Declared current exposure to passive smoking									
No		63 (36.2%)	2 (11.1%)	1.00 (Ref.)	–	530 (51.7%)	122 (43.3%)	1.00 (Ref.)	–
Yes		111 (63.8%)	16 (88.9%)	4.541 (1.011–20.393)	0.048*	496 (48.3%)	160 (56.7%)	1.401 (1.075–1.828)	0.013*
Alcohol intake									
No		159 (91.4%)	16 (88.9%)	1.00 (Ref.)	–	937 (91.3%)	255 (90.4%)	1.00 (Ref.)	–
Current drinker		15 (8.6%)	2 (11.1%)	1.325 (0.278–6.321)	0.724	89 (8.7%)	27 (9.6%)	1.115 (0.709–1.752)	0.638
Declared exposure to pollution									
No		76 (43.7%)	6 (33.3%)	1.00 (Ref.)	–	393 (38.3%)	96 (34.0%)	1.00 (Ref.)	–
Yes		98 (56.3%)	12 (66.7%)	1.551 (0.557–4.322)	0.401	633 (61.7%)	186 (66.0%)	1.203 (0.912–1.586)	0.191
LMDS (mean ± SD)	0.602	38.63 ± 5.36	38.83 ± 5.54	1.007 (0.920–1.102)	0.876	40.59 ± 4.98	39.57 ± 5.65	0.962 (0.937–0.987)	0.004*
BDS-22 (mean ± SD)	0.981	12.39 ± 13.82	11.89 ± 14.10	0.997 (0.962–1.034)	0.987	10.62 ± 13.61	12.91 ± 15.99	1.011 (1.002–1.020)	0.028*
Depression		3.44 ± 4.01	3.22 ± 4.07	0.986 (0.870–1.117)	0.956	2.91 ± 3.86	3.54 ± 4.65	1.037 (1.005–1.069)	0.039*
Demotivation		1.83 ± 2.78	1.67 ± 2.70	0.978 (0.815–1.174)	0.810	1.48 ± 2.60	1.90 ± 3.20	1.052 (1.005–1.100)	0.051
Psychosomatic		2.09 ± 2.72	1.94 ± 2.88	0.981 (0.816–1.178)	0.688	1.78 ± 2.65	2.11 ± 2.94	1.043 (0.995–1.092)	0.097
Mood deterioration		2.41 ± 2.35	2.06 ± 2.04	0.934 (0.752–1.161)	0.657	1.98 ± 2.25	2.33 ± 2.50	1.066 (1.009–1.126)	0.033*
Intellectual inhibition		1.36 ± 2.05	1.61 ± 2.00	1.058 (0.846–1.323)	0.265	1.27 ± 1.96	1.59 ± 2.40	1.073 (1.010–1.140)	0.040*
Anxiety		1.26 ± 1.60	1.39 ± 1.42	1.050 (0.778–1.418)	0.563	1.19 ± 1.59	1.46 ± 1.72	1.102 (1.019–1.192)	0.020*
LMAS (mean ± SD) [for 1257 patients under medical treatment]	0.870	12.59 ± 2.62	12.71 ± 2.13	1.021 (0.807–1.292)	0.904	12.83 ± 2.25	12.46 ± 2.78	0.942 (0.894–0.994)	0.048*
Occupational factor		4.41 ± 1.06	4.50 ± 0.94	1.092 (0.609–1.957)	0.848	4.52 ± 0.93	4.38 ± 1.03	0.875 (0.764–1.001)	0.065
Psychological factor		3.66 ± 0.89	3.79 ± 0.80	1.218 (0.561–2.647)	0.515	3.77 ± 0.81	3.65 ± 1.00	0.862 (0.746–0.997)	0.072
Annoyance factor		2.73 ± 0.68	2.86 ± 0.36	1.513 (0.454–5.039)	0.702	2.80 ± 0.61	2.72 ± 0.75	0.842 (0.692–1.025)	0.123
Economical factor		1.79 ± 0.62	1.57 ± 0.85	0.659 (0.319–1.362)	0.252	1.75 ± 0.67	1.71 ± 0.71	0.916 (0.753–1.115)	0.383
IPAQ n (%)	0.587								
No/or low physical activity		34 (19.5%)	7 (38.9%)	1 (Ref.)	–	442 (43.1%)	153 (54.3%)	1 (Ref.)	–
Moderate physical activity		91 (52.3%)	10 (55.6%)	0.534 (0.188–1.515)	0.238	463 (45.1%)	113 (40.1%)	0.705 (0.535–0.929)	0.013*
High physical activity		49 (28.2%)	1 (5.6%)	0.099 (0.012–0.843)	0.034*	121 (11.8%)	16 (5.7%)	0.382 (0.220–0.664)	0.001*
Total sitting time/day, min (mean ± SD)		369.43 ± 180.61	447.14 ± 228.42	1.002 (1.000–1.005)	0.139	504.02 ± 199.96	530.12 ± 203.66	1.001 (1.000–1.001)	0.053

Notes: Data are presented as count (%) or mean ± standard deviation (SD). *P <0.05 was considered significant.

Abbreviations: OR, odds ratio; CI, confidence interval; LMDS, Lebanese Mediterranean diet score; BDS-22, Beirut Distress Scale; LMAS, Lebanese Medication adherence scale; IPAQ, International Physical Activity Questionnaire.

Conversely, adherence to LMDS appeared to be responsible for a significant reduction of approximately 4% in odds of CHD in post-menopausal women for each one-unit increase in LMDS (OR: 0.962 [0.937–0.987]).

Psychological distress was found to be more frequent for coronary postmenopausal women, with a remarkable internal consistency (alpha's Cronbach: 0.981) specifically in the depression (OR: 1.037 [1.005–1.069]), mood deterioration (OR: 1.066 [1.009–1.126]), intellectual inhibition (OR: 1.073 [1.010–1.140]) and anxiety domains (OR: 1.102 [1.019–1.192]).

Medication adherence, assessed by LMAS (with excellent internal consistency, alpha's Cronbach=0.87), was significant only for the post-menopausal group among the 1257 studied women under medical treatment, revealing a reduction of about 6% in odds of CHD.

Concerning PA, more than half of coronary post-menopausal women reported exercising a little or not at all (54.3%), while PA seemed to be associated with a significant decrease in odds of CHD: moderate PA showed a 29.5% reduction in odds of CHD, and high PA a 61.8% decrease, compared to no or low PA (OR: 0.705 [0.535–0.929] or 0.382 [0.220–0.664] respectively). While, for pre-menopausal women, high PA alone was found to be significant in protecting against CHD (OR: 0.099 [0.012–0.843]).

Independent Predictors of CHD

Dyslipidemia (aOR: 6.938 [1.835–26.224], p=0.004), hypertension (aOR: 6.195 [1.318–29.119], p=0.021), family histories of dyslipidemia (aOR: 6.143 [1.560–24.191], p=0.009) and premature CHD (aOR: 4.739 [1.336–16.805], p=0.016) were the only RFs associated with CHD in pre-menopausal women.

Dyslipidemia (aOR: 3.018 [2.102–4.332], p<0.001), hypertension (aOR: 2.449 [1.386–4.327], p=0.002), family history of premature CHD (aOR: 2.724 [1.949–3.808], p<0.001), cumulative cigarette smoking (aOR: 2.317 [1.574–3.410], p<0.001), and joint pain (aOR: 1.457 [1.053–2.016], p=0.023) were the independent RFs for CHD in post-menopausal women, while an inverse association was found between CHD and living in Mount-Lebanon (compared to Beirut, aOR: 0.589 [0.406–0.854], p=0.005), having a moderate individual monthly income (aOR: 0.450 [0.220–0.923], p=0.029), following the Mediterranean diet (aOR: 0.965 [0.936–0.994], p=0.020), and PA (aOR: 0.725 [0.529–0.992] and 0.396 [0.206–0.759], for moderate and high PA, respectively, p=0.007) (Table 4).

Another protective factor assessed, LMAS, was not significantly associated with CHD at this stage.

Discussion

This is, to our knowledge, the first case-control study conducted to assess RFs of CHD among hospitalized Lebanese women and we hope that the results found will help shed light on a currently not yet sufficiently studied problem concerning the cardiovascular health of aging women. This study was conducted to further clarify the nature of CHD RFs in Lebanese women, not only the elderly but also those of reproductive age. It is not uncommon nowadays to see pre-menopausal women admitted with CHD.

Common coronary RFs were noted, but their relative importance differed in pre- and post-menopausal women. Dyslipidemia was found to be associated with the highest odds ratio in both groups, consistent with previous works, showing that dyslipidemia has the greatest population-adjusted risk in women compared to all other known CVRFs.[25] In contrast, other studies in South Asia found a statistically significant relationship in post-menopausal women only,[26] which could be explained by their sample size and the younger age of pre-menopausal women included in their study (30 years and older). On another hand, previous data showed that 3.9 million worldwide deaths were attributable to high non-HDLc in 2017, increasing among women since 1980,[27] and it is actually well known that lipid levels change in post-menopausal women after reduction of estrogen production (decline in HDLc and increase in LDLc), subsequently contributing to an increased CHD risk.[28,29] Moreover, Lebanon has the highest prevalence of hypercholesterolemia[30] compared with other countries such as Turkey, Saudi Arabia and India. Also, it has been found that Lebanese women were more likely to suffer from dyslipidemia than men.[9]

Hypertension was also significantly associated with CHD in both groups which correlates well with the findings of Gierach et al and Maas et al[31,32] Our findings underscore the importance of early identification of hypertension in middle-aged women as a first step in the evaluation and treatment of CHD in the premenopausal period, as each 10 mmHg increment of systolic

Table 4 Factors Believed to Be Associated with Cardiovascular Risk for the Women Studied

Predictors	P-value	aOR[a]	95% CI
Model 1: among pre-menopausal women			
Dyslipidemia	0.004*	6.938	1.835–26.224
Hypertension	0.021*	6.195	1.318–29.119
Family history of dyslipidemia	0.009*	6.143	1.560–24.191
Family history of premature CHD	0.016*	4.739	1.336–16.805
Model 2: among post-menopausal women			
Dyslipidemia	<0.001*	3.018	2.102–4.332
Hypertension	0.002*	2.449	1.386–4.327
Family history of premature CHD	<0.001*	2.724	1.949–3.808
Cigarette smoking, quantification			
Non-smoker (reference)	<0.001*	–	–
Up to 20 pack-years	0.818	1.061	0.639–1.763
More than 20 up to 40 pack-years	0.005*	1.881	1.206–2.935
More than 40 pack-years	<0.001*	2.317	1.574–3.410
Declared joint pain	0.023*	1.457	1.053–2.016
Monthly income per individual			
Low (<180,000 LBP/month/person)/Reference	0.070	–	–
Middle (180,000–675,000 LBP/month/person)	0.029*	0.450	0.220–0.923
High (>675,000 LBP/month/person)	0.110	0.540	0.254–1.149
Place of residence			
Beirut (Reference)	0.014*	–	–
Mount Lebanon (peri-urban area)	0.005*	0.589	0.406–0.854
South Lebanon/Nabatieh (rural area dominance)	0.787	0.919	0.497–1.700
North/Akkar (rural area dominance)	0.221	0.728	0.438–1.210
Bekaa/Baalback/Hermel (rural area dominance)	0.496	1.198	0.713–2.013
IPAQ			
No/or low physical activity (Reference)	0.007*	–	–
Moderate physical activity	0.045*	0.725	0.529–0.992
High physical activity	0.005*	0.396	0.206–0.759
LMAS	0.088	0.950	0.895–1.008
LMDS	0.020*	0.965	0.936–0.994

Notes: [a]Odds ratios were adjusted by regression analyses for all possible confounders (particularly age). *P <0.05 was considered significant. Regression model 1 included the following variables: age, educational level, cigarette smoking-quantification, hypertension, diabetes, dyslipidemia, declared joint pain, family histories of premature CHD and dyslipidemia, declared current exposure to passive smoking, IPAQ and sedentary time. Regression model 2 included the following variables: age, place of residence, marital status, educational level, monthly income per individual, cigarette smoking-quantification, waterpipe smoking-quantification, hypertension, diabetes, dyslipidemia, declared joint pain, family histories of premature CHD and HTN, declared current exposure to passive smoking, declared exposure to pollution, LMDS, BDS-22, LMAS, IPAQ and sedentary time. The model was suitable and Hosmer-Lemeshow test was adequate (p>0.05). Absence of multi-collinearity between predictors (correlation coefficients <0.8).

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; CHD, coronary heart disease; LBP, Lebanese pounds; LMDS, Lebanese Mediterranean Diet Score; IPAQ, International Physical Activity Questionnaire; BDS-22, Beirut Distress Scale; LMAS, Lebanese Medication Adherence Scale.

blood pressure was found to be associated with a 25% increased risk of cardiovascular events.[4] While hypertension prevalence and severity reach significantly higher rates in women than men over 65, this gap is likely to increase with the aging population.[4] A systematic review showed that the hypertension prevalence occurs more frequently among Arab women,[33] and is increasing in Lebanon.[9] Moreover, women appear to have lower rates of hypertension control than men,[34,35] including in Lebanon.[36] This could be due to the political instability and various conflicts that have occurred in recent years in Lebanon. Previous studies have demonstrated the importance of stress exposure (war, disaster, explosion and terror) on blood pressure levels and hypertension control, especially among women.[37]

Similar to previous studies,[13] we found that family history of premature CHD increased the CHD risk. It is an independent prognostic indicator, and early detection of silent atherosclerosis may usefully improve the CHD prevention in concerned women. Additionally, a first-degree family history of dyslipidemia predicted CHD in the premenopausal group, which could also help to better identify high-risk women and potentially initiate or intensify CHD prevention strategies.

Smoking, an avoidable factor that appeared to have a multiplicator effect with the other major CHD RFs,[4] was well correlated with postmenopausal women's CHD, with a known cumulative deleterious effect in our study as previously described.[38] A meta-analysis reported that women had a 25% increased risk of smoking-induced CHD compared to men.[39] However, the harmful impact of smoking in CHD is underestimated, especially in low- and middle-income countries, and real risk on women's health could be higher.[39] Unfortunately, Lebanese women exhibit the highest rates of smoking prevalence of the Middle Eastern countries, due to its liberal character, westernization and the lessening of cultural constraints on women's behavior.[40] WHO reported that about one-third of women in Lebanon use tobacco, compared to 6% in Jordan, a demographic group that could greatly benefit from control initiatives.[41,42] However, it seems that implementing such tobacco control programs may be a challenge in Lebanon, given that a recent ban on smoking in public areas has been largely ignored.[41]

A socio-economic gradient in heart disease, previously reported in wealthy, mainly Western countries, is also discernible in Lebanon.[43] In fact, the economic factor was inversely associated with CHD, consistent with population-based studies from Lebanon.[8] It suggests that among residents of Lebanon, a middle-income developing country, women with moderate monthly income level have lower odds of CHD than those with a lower monthly income level. However, the higher income level, although achieving an odds ratio<1, did not reach statistical significance, perhaps due to the small (but representative) sample size in this category.

Living in the capital Beirut (crowded urban area) compared to Mount-Lebanon (peri-urban area) was positively associated to CHD. Living in Beirut exposes participants to higher levels of stress, in part due to exposure to various environmental factors, traffic-related air pollutants, noise, higher levels of violence, and lower social support, consistent with previous national[8,9] and international[44,45] studies. Similarly, the lack of green spaces in an urban area can negatively affect a person's well-being and PA.[46] Previous works revealed that women may be more vulnerable to urbanization in terms of CVRFs (hypertension, psychiatric disorders) than men.[7,47,48] Further national analysis will be needed to elucidate the effect of urban environment in Lebanon on cardiovascular health in both genders.

Adherence to LMDS was associated with lower odds of CHD in postmenopausal women, in agreement with previous national studies.[49] This relation was also described in recent studies, where adopting a Mediterranean diet pattern was related to improved arterial stiffness and reduced risk of chronic diseases.[50,51] Bihuniak et al also demonstrated positive associations between the Mediterranean diet and health of postmenopausal American women, particularly with a reduced risk of CVRFs.[52] Furthermore, women adhering to the Mediterranean diet may have better CVRFs protection than men (21% vs 14% respectively).[53] Unfortunately, a deviation in dietary habits exists in Lebanon, as in all transitional countries adopting a more Westernized lifestyle.

Moreover, our results showed that moderate or vigorous PA had an inverse association with CHD in women compared to those with no or low PA. This is consistent with data in favor of a substantial reduction in the incidence of cardiovascular events by PA in postmenopausal women.[54,55] We also demonstrated an inverse dose-response relationship, with higher activity levels being associated with lower CHD, in agreement with several previous reports.[56] However, an overview of systematic reviews and meta-analysis from 20 MENA (Middle East and North Africa) countries revealed that only the adult Lebanese and Jordanian women were more active than men compared to other regions.[55] Urbanization, residence in Beirut, car ownership, and obstacles in some areas of Lebanon's governorates, mainly rural villages, where it is socially unacceptable for women to walk or exercise alone outside the home without the company of a family member, may affect their PA.[57,58] In our study, 93% of postmenopausal women were unemployed, factor that may be of importance in physical engagement of women,[59] we can deduce that the domestic activity could protect from CHD by fighting against sedentary lifestyle, as has been mentioned by others.[60]

Finally, an enlightening result of our study was the significant link between CHD and the presence of joint pain. Studied postmenopausal women who suffer from it were almost 1.5 times more likely to have CHD than those without. Thus, this disorder, which increases with age, especially in menopause,[61] can not only affect the daily life of aging women, it also limits their PA,[62] which increases the CVD risk, therefore has an impact on women's life expectancy. Additionally, evidence shows that chronic diseases and musculoskeletal disorders frequently coexist; people with musculoskeletal problems are about twice as likely to suffer from chronic diseases such as heart disease, gastric ulcers, neurological and endocrine disorders.[63] Other evidence also suggests that this relation is biologically plausible, as daily

back pain was associated with reduced quality of life, mobility and longevity and increased risk of coronary events in elderly women.[64] Relation between rheumatoid arthritis and heart disease is described,[65,66] but very few studies focus on commonplace joint pain.[67] A previous study reported that over half (56%) of CHD patients suffered from musculoskeletal conditions, with joint pain accounting for 64.4% of them.[61] Joint pain in aging women seems harmless and is thus probably neglected by women, while it could constitute a medical warning sign for them and their attending physicians.

Strengths and Limitations

This study has several strengths in its design: the random selection of controls minimizes associated biases; also, the use of incident cases allows more accurate recall of past exposures, helps with temporality and avoids survival bias. The relatively large number of participants and the choice of a control/case ratio of 4/1 increased its power. However, it is a retrospective observational study that cannot determine causality between factors and disease occurrence. Otherwise, evaluation of some RFs and preventive measures were self-declared, which could lead to misclassification. A differential recall bias could be present, as CHD patients were more likely to remember accurately their exposures' history compared to non-coronary patients. Finally, although we considered many RFs to decrease potential confounding, residual confounding might still be possible, related to unmeasured factors.

Conclusion

The study of CVRFs in women is a necessity since they are well affected by CHD. Improved screening and therapeutic management of arterial hypertension and dyslipidemia in this population is needed. It is necessary to intensify the fight against smoking and encourage women to adhere to a Mediterranean diet. Screening mechanisms for silent atherosclerosis in women with a family history of premature CHD, increased awareness of dwelling region and reduction of poverty are also important steps. Moreover, the common joint pain, often trivialized and neglected in menopaused women, could be integrated in prevention strategies and dedicated care. Women in pre-menopause could benefit from a dedicated information program aimed at not trivializing this symptom, probably associated with other deleterious elements such as less PA and a more sedentary lifestyle. Taken together, these findings highlight the importance of formulating appropriate policies and implementing interventions to halt the CHD progression in Lebanese women. Thus, the role of policymakers and health providers, in cooperation with the ministry of public health and non-governmental organizations, to provide quality services and to raise awareness in women to lower the burden of the disease.

Abbreviations

aOR, adjusted odds ratio; BDS-22, Beirut Distress Scale; BMI, body mass index; CHD, coronary heart disease; CI, confidence interval; CVD, cardiovascular disease; CVRFs, cardiovascular risk factors; HDLc, high-density lipoprotein cholesterol; IPAQ, International Physical Activity Questionnaire; LDLc, low-density lipoprotein cholesterol; LMAS, Lebanese Medication Adherence Scale; LMDS, Lebanese Mediterranean Diet Score; MET, metabolic equivalent; MI, myocardial infarction; OR, odds ratio; PA, physical activity; RFs, risk factors; SPSS, Statistical Package for the Social Sciences; WHO, World Health Organization.

Data Sharing Statement

The data can be made available upon reasonable request to the corresponding author.

Ethics Approval and Informed Consent

The study protocol was reviewed and approved by the Institutional Review Board (IRB) ethical committee of each participating hospital, in accordance with Lebanon's ethical legislation, and the Declaration of Helsinki. The informed consent process was confirmed by the IRB and obtained from all participants before the interview. Patients were informed that their response will be kept confidential.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting the article or reviewing it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to take responsibility and be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no conflicts of interest for this work.

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