Biochemical Markers, Body Composition and Risk of Cardiovascular Disease Amongst Geriatric Population in Al Madinah Al Munawarah: A Risk Assessment Study

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Abstract

Objective: to assess selected biochemical markers and body composition and their association with CVD risk amongst older adults in Al Madinah Al Munawarah, Saudi Arabia.

Results: Older adults had high glycated hemoglobin percent (women 7•90±2•95; men 8•4±1•64, P <0•001), C-reactive protein (women 17•1±5•92; men 36•1±7•8, P <0•003) and Atherogenic Index of Plasma (AIP; women 0•21±0•18; men 0•22±0•21, P <0•04) with higher values amongst men compared to their counterparts. In addition, they suffered from hypoalbuminemia and low hemoglobin levels. Older adults were malnourished, either underweight (16%) or overweight and obese (35%). Based on their AIP, most of the participants had intermediate to high CVD risk. Multiple Linear Regression model with age as the dependent variable showed that the risk of CVD increased with higher BMI (women only: Odd ratio 6.99, 95% CI: 0.96-5.03, P <0.001), elevated triglycerides (women: Odd ratio 7.47, 95% CI: 0.16-3.17; men: Odd ratio: 6.55, 95% CI: 0.23-3.26, P <0.001), high C-reactive protein (Odd ratio 8.99, 95% CI: 0.99-6.00, P = 0.003; men: Odd ratio 4.00, 95% CI: 0.99-3.01, P < 0.002) and high AIP (women: Odd ratio 14.6, 95% CI: 0.0.56-16.18, P = 0.002; men: Odd ratio 7.35, 95% CI: 0.35-20.29, P < 0.001).

Introduction

The ageing process involves various physical and physiological changes including metabolic, neurological and immunological changes.[1] Cardiovascular diseases (CVDs) are amongst the most-life threatening diseases worldwide and increase the risk of morbidity and mortality amongst aging adults. Although, the prevalence of patients with CVDs is 42,790 and 50,213 for women and men respectively,[2] little is known about the risk among the Saudi older adults.

Traditionally, obesity,[3−6] elevated blood pressure,[7−8] lipid profile (including total cholesterol, low- and high-density lipoprotein cholesterol[9−10] (LDL-C, HDL-C) and triglycerides concentrations), impaired fasting glucose and diabetes are the predictors of CVD risk, morbidity and mortality.[11−13] Furthermore, serum proteins such as albumin and prealbumin are used to define the nutritional status of adults and predict CVD risk.[14]•

Non-traditional CVD risk factors include deficiencies of vitamins such as B_{12}, B_6, and folate, due to their association with hyperhomocysteinemia, a vascular risk factor that increases the risk of coronary heart disease.[15] In addition, an increase in the inflammatory marker C-reactive proteins is an indication of cognitive and physical impairments and is being reported as a crucial predictor of CVD risk and reduced survival amongst older adults.[16] Moreover, the Atherogenic Index of Plasma (AIP) which is the logarithm of triglycerides to HDL-C ratio, is shown to be a good predictor of the risk of all-cause deaths amongst the older adults and a useful non-traditional indicator for CVD risk.[17−18]

The determination of selected CVD risk factors helps in identifying those older adults who are at increased risk of morbidity and mortality, hence developing appropriate programs in the country. The current study aimed to determine the body composition, selected biochemical markers and CVD risk amongst free-living older Saudi men and women. It is hypothesized that older persons are at increased risk of CVD.

Methods

An epidemiological, cross sectional study was conducted between January 2018 to January 2020 targeting Saudi older aged $\geq$ 65 years old living in Al Madinah Al Munawarah city with no history of myocardial infarction or stroke recruited from various community settings e.g. Mosques (for men) and religious schools (men and women). Relatives, friends and neighbors were also invited to participate. The sample size was determined based on the following equation:

$$n = (Z_{1-\alpha/2})^2 \text{x P (1-P)} \div d^2$$

Considering a confidence level of 95%, $Z_{1-\alpha/2}=1\bullet96$, d = 0•05 and using a 3•5% malnutrition prevalence in this population.[19]

Data Collection

Socio-demographic data collected included age, gender, marital status, educational status, and smoking habits. Information was also obtained about the presence or history of diseases. Weight and height were measured twice using an electronic scale (Beurer GmbH Type PS 07, China) and BMI was calculated. Blood samples (5 ml) were collected in plain and EDTA tubes and tests were done using the clinical chemistry automated machine Dimension X P and, Siemens Healthcare Diagnostics Ltd Frimley, Camberley, UK. The Atherogenic Index of Plasma (AIP) = log (TG/HDL-C) was calculated as an Atherogenic dyslipidemia index. Moreover, N-MID (Roche diagnostics, GmbH, Mannheim, German) and the Cobas e 411 immunoassay analyzer (Roch Diagnostics, GmbH, German) were used. The assay was based on chemiluminescence–immunoassay technology according to the manufacturer's instructions.

Statistical analysis:

Statistical analysis was performed by the software package known as Graphpad Prism 7 (GraphPad Software, CA, USA). Differences between older men and women were analyzed using Independent Student's *t*-test. Analysis of variance (ANOVA) analysis was used to find differences amongst selected biochemical markers and AIP categories. Pearson's correlation was used to determine the association between AIP and selected CVD risk factors. Multivariate analysis based on Multiple Linear Regression model was run to predict risk of CVD for older adults. Significance level was set at < 5%.

Results

Older adults (n = 600) aged 65–90 years were included in the study with equal numbers of men and women. Their mean BMI was normal and most of them were married, had schooling education, living with their families and were non-smokers. In addition, more older men were employed (P = 0•04) and diabetic (P = 0•05) whereas more women were hypertensive (Table 1).

Table 1
Socio-demographic characteristics of older adults. Numbers, percentages and P-values are shown

Variables	Women (n = 300)	Men (n = 300)	P-value
	n (%)	n (%)	
Age in years			
Mean ± SD	74•5 ± 32•8	77 ± 55•8	0•08
BMI (Kg/m^2)			
Mean ± SD	23•48 ± 3•69	22•18 ± 9•05	0•11
Marital status:			0•72
- Married	226 (75•3)	233 (77•6)	
- Widow	13 (4•3)	17 (5•7)	
- Divorced	37 (12•3)	30 (10)	
- Single	24 (8)	21 (7)	
Educational level:			0•84
- Religious schools or illiterate	45 (15)	30 (10)	
- Primary /secondary or senior school	165 (55)	150 (50)	
- University education	90 (30)	120 (40)	
Employment status:			**0•04***
- Employed	120 (40)	167 (55•7)	
- Unemployed (retired)	180 (60)	134 (44•7)	
Living status:			0•85
- Living alone	16 (5•3)	32 (10•7)	
- Living with family or relatives	284 (94•7)	268 (89•3)	
Smoking habit:			
- Smoker**s**	11 (3•7)	92 (30•7)	**0•001****
Presence of chronic disease:			
- No chronic disease	17 (5•7)	9 (3)	0•88
- Diabetes Mellitus	216 (72)	248 (82•7)	**0•05***
- Hypertension	46 (15•3)	33 (11)	**0•04***

Variables	Women (n = 300)	Men (n = 300)	P-value
- Others§	21 (7)	10 (3•4)	0•85

P-value obtained from Independent Student t-test• *p < 0•05, **p < 0•001•

§ *Others included having more than one health problem and those with other diseases such as thyroid disorders, osteoporosis, gastrointestinal disorders, etc.•*

When compared with normal laboratory values, the study indicated that both older men and women had higher fasting blood glucose, glycated hemoglobin A1C, total serum cholesterol, C-reactive proteins levels and AIP. On the other hand, they had lower hemoglobin, serum iron, serum albumin and vitamin B_{12} levels (Table 2). Although these biochemical markers are elevated for the older participants, women had better values than their counterparts in some of these markers.

Table 2: Selected Biochemical markers for older Saudi men and women. Mean ± SD, normal and P-values are shown

Blood Test	Women (n = 300)	Men (n = 300)	P-value	Normal values
Fasting Blood Glucose (mmol/L)	5•77 ± 5•76	6•23 ± 4•32	0•40	4•6−6•4
Glycated Hemoglobin A1C (%)	7•90 ± 2•95	8•4 ± 1•64	< 0•001**	4•3−6•0
Hemoglobin level (g/dl)	12•6 ± 3•46	12•6 ± 3•46	0•27	12−16
Iron (µmol/L)	7•8 ± 9•83	9•8 ± 3•73	0•80	9•0−30•4
Ferritin ug/mL	68•12 ± 14•705	39•12 ± 12•991	< 0•001**	12 to 150
LDL-cholesterol (mmol/L)	3•23 ± 0•86	2•92 ± 1•02	0•87	5•2−6•1
HDL-cholesterol (mmol/L)	1•22 ± 0•31	1•02 ± 0•19	< 0•001**	1•0
Total cholesterol (mmol/L)	6•78 ± 1•14	6•63 ± 1•13	0•04*	5•3−6•2
Triglycerides (mmol/L)	1•27 ± 0•67	1•49 ± 1•1	< 0•001**	0•40 − 1•52
ALT (U/L)	16 ± 2•01	18 ± 4•01	0•01*	7−55
AST (U/L)	20•0 ± 9•18	19•0 ± 6•18	0•06	15•1−46•2
Creatinine (mmol/L)	57•1 ± 9•83	89•1 ± 10•33	< 0•001**	45−90
C-reactive protein (mg/L)	17•14 ± 5•92	36•14 ± 7•82	0•003**	0•00−5•00
AIP	0•21 ± 0•18	0•22 ± 0•21	0•04*	0•11 − 0•21
Albumin (g/L)	33•0 ± 5•21	37•0 ± 7•31	0•02*	35−55
Vitamin B$_{12}$ (pmol/L)	220•0 ± 22•80	215 ± 22•78	< 0•05*	118−701

*P-value obtained from Independent Student t-test• *p < 0•05, **p ≤ 0•001•*

Results further revealed that more men (44%) than women (26•4%) were either overweight and/or obese. On the contrary, hypoalbuminemia was more common among women (54%) than men (41%). Based on their AIP results, the prevalence of intermediate to high CVD risk amongst men was significantly higher than women (55% versus 94%, P = 0•003). Men (57%) and women (33%) also had high C-reactive protein levels (Table 3).

	Women n (%)	Men n (%)
Table 3: Categories of Body composition and selected biochemical markers amongst Saudi old men and women. Number and percentages are shown#		
BMI (Kg/m^2)		
Underweight (< 18•5)	74 (24•7)	23 (7•7)
Normal weight (18•5 to 25)	149 (49•7)	125 (41•7)
Overweight (25 to 29•9)	68 (22•7)	110 (36•7)*
Obese (≥ 30)	11 (2•7)	22 (7•3)
Albumin (g/L)		
< 35	163 (54•3)	122 (40•7)
35−50	126 (42•0)	177 (59•0)
> 50	9 (3•0)	1 (0•3)*
Hemoglobin (g/dl)		
F < 12 g/dl; M < 14	122 (40•7)	162 (54)
F 12 to 16; M 14 to 18	176 (58•7)	135 (45)
F > 16; M < 18	2 (0•7)	3 (1)
Iron (µmol/L)		
F < 11; M < 14	201 (67•0)	253 (84•3)
F 11−29; M 14−32	90 (30•0)	49 (16•3)
F > 29; M > 32	9 (3•0)	0 (0)**
Glycated hemoglobin A1C (%)		
Normal < 5•7	60 (20•0)	17 (5•7)
Pre-diabetic 5•7% to 6•4	24 (8•0)	35 (11•7)
Diabetic > 6•4	216 (72•0)	248 (82•7)*
Vitamin B$_{12}$ (pmol/l)		
< 118	73 (24•3)	25 (8•3)*
118−701	211 (70•3)	251 (83•7)

#*Total number of women (300) and men (300); P-value obtained from One-way ANOVA• *P < 0•05; **p < 0•001*

Table 3: Categories of Body composition and selected biochemical markers amongst Saudi old men and women. Number and percentages are shown[#]		
> 701	16 (5•3)	**24 (8)**
Atherogenic Index of Plasma (CVD risk)		
Low	135 (45)	**18 (6•0)**
Intermediate	77 (25•7)	**5 (1•7)***
High	88 (29•3)	**277 (92•3)****
C-reactive protein (mg/L)		
< 1•00 mg/L	50 (16•6)	**20 (6•7)**
1•00−5•00 mg/L	150 (50•0)	**110 (36•7)**
> 5 mg/L	100 (33•4)	**170 (56•6)***

[#]*Total number of women (300) and men (300); P-value obtained from One-way ANOVA• *P < 0•05; **p < 0•001*

Moreover, both older men and women with high CVD risk based on AIP, had significantly elevated fasting blood glucose (women only), glycated hemoglobin A1C, LDL-C, total cholesterol, triglycerides, C-reactive protein, serum iron (women only) and albumin levels as well as were obese (Supplementary Table 1). Furthermore, using Pearson's correlation, high CVD risk based on their AIP associated positively with triglycerides (r = 0•76, P = 0•003), total cholesterol (men only: r = 0•56, P = 0•02), LDL-C (men only: r = 0•62, P = 0•001), C-reactive proteins (r = 0•50, P = 0•03) and BMI (women only: r = 0•81, P = 0•002). In addition, high AIP correlated negatively with albumin levels (r = -0•62, P = 0•01) and HDL-C (men only: r= -0•57, P = 0•05). Results not shown on Table.

Multivariate analysis based on the Multiple Regression in which age was the dependent variable and the biochemical markers, AIP and BMI were the independent variables revealed higher significant odds for BMI, triglycerides, C-reactive protein, and AIP (Supplementary Table 2).

Discussion

Although older adults are at increased risk of CVD, few studies were published focusing on the major risk factors in Al Madinah Al Munawarah. The current study revealed that older adults are at increased risk of CVD based on selected traditional and non-traditional risk factors. Thus, the study hypothesis was accepted. The current study revealed that older women and men had intermediate to high CVD risk based on their AIP values. The use of AIP as an atherogenic index is a strong predictor of myocardial infarction and atherosclerosis and the study findings supported other studies which indicated that high AIP is

directly associated with older age,[20–21] and could be used as a stand-alone index for cardiac risk estimation.[17–21]

Furthermore, studies indicated that serum albumin is inversely related to inflammatory processes,[13] and hypoalbuminemia is strongly correlated with all-cause mortality and cardiovascular mortality.[22] The current study revealed that a significant number of Saudi men (41%) and women (54%) had hypoalbuminemia. Previous studies have indicated that serum albumin is significantly correlated with steps per day and physical activity.[23] Physical inactivity is very common amongst Saudi older adults and among other problems such as low protein intake,[19] could have resulted in the low serum albumin levels.

Moreover, C-reactive protein has a direct role in promoting vascular inflammation, vessel damage and clinical CVD events and can predict the long-term risk of myocardial infarction and sudden cardiac death in healthy people.[16] The current study showed that on average both older men and women had significantly elevated C-reactive protein values with 33% of the women and 57% of the men having very high levels. In addition, high AIPs among Saudi older adults significantly correlated with high C-reactive protein levels and this is true irrespective of the gender. Studies revealed that high C-reactive protein values are associated with a high global cardiovascular risk.[16]

Moreover, it is well known that diabetes mellitus is an independent risk factor for CVD.[11–12] Meta-analysis and systemic reviews revealed that diabetes increases CVD risk by approximately twofold especially amongst those who are known diabetic compared to newly diagnosed diabetics.[24] The current study supported this theory and revealed that most of the older men and women were already diabetic and their fasting blood glucose and glycated hemoglobin A1C were elevated (Table 2). Older adults with high risk of CVD based on their AIP also had higher glycated hemoglobin A1C although this association didn't reach to significance level in the Multiple Regression model.

Furthermore, previous studies conducted in Saudi Arabia reported that the prevalence of anemia among older adults is 13–18% with women more affected than men.[25] Hemoglobin concentration could influence the cardiovascular system via oxygen supply and blood viscosity and anemia is shown to be an independent risk factor for CVD.[26] The current study showed that both older men and women had low hemoglobin and serum iron levels (Table 2). The prevalence of anemia is very high and women with high risk for developing CVD as defined by high AIP, had the lowest serum iron levels (Supplementary Table 1).

One of the independent risk factors associated with the development of CVD is increased body weight which affects hemodynamics and heart structure.[3–6] The current study found a significant number of older men and women being either overweight or obese; with men being more affected by the problem. Amongst women, high AIP values were significantly associated with high BMI (r = 0•81, P = 0•002) and those with lower AIPs have either normal weight (women) or overweight (men). A previous study conducted in Al Madinah Al Munawarah on older adults revealed that the prevalence of obesity and

overweight combined was 78% and 83% among older men and women respectively.[19] One of the main reasons for the increased body weight in this community is the sedentary lifestyle and high carbohydrate intakes.

In conclusion, Saudi older men and women had increased risk for developing CVD based on their odd ratios and high prevalence of traditional and non-traditional risk factors. Based on the findings of the current study, urgent community-intervention programs should target older adults in Al Madinah Al Munawarah.

Limitations Of The Study

Although it is considered the first study to be carried out in geriatric population in Al Madinah Al Munawarah, there are still some limitations for our findings.

- The cross-sectional nature of the study design has its draw backs and potential bias and thus findings should be interpreted with caution. Ideally, it would have been more appropriate to conduct a longitudinal study to follow up those older adults for a certain period and report the actual risks for developing CVD based on traditional and non-traditional risk factors.
- In addition, the selection of sample was a convenient sampling method which means the study lost its randomization and as such generalization of the findings would be questioned. However, since it was not possible to obtain a representative sample through a computerized system, non-randomized sampling method was the most appropriate solution.
- Also, blood samples were only taken once, and this might have introduced bias due to the day to day variations. However, the inclusion of a large sample size at 95% confidence interval might have reduced this bias.

Abbreviations

AIP
Atherogenic Index of Plasma
ALT
Alanine transaminase
AST
Aspartate transaminase
BMI
Body Mass Index
CI
Confidence Interval
CVD
Cardiovascular diseases
HDL-C

High density lipoprotein cholesterol
LDL-C
Low density lipoprotein cholesterol
WHO
World Health Organization

Declarations

• Ethics approval and consent to participate:

Ethical permission was obtained from the ethical committee at the Faculty of Applied Medical Sciences (Approval # **CLN 201703)**, Taibah University in Al Madinah Al Munawarah where the researchers are currently employed. Signed consent was also sought from older adults (A copy of the consent form is available upon request).

• Consent to publish:

Included in the consent to participate form

• Availability of data and materials:

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

• Competing interests:

The authors declare that they have no competing interests.

• Funding:

The study was self-funded by the authors.

• Authors' Contributions:

WM (The 1st author): Laboratory work, Data entry and analysis, Part of the methodology Writing part of the result section.

AE (The corresponding author): Body composition measurements, Manuscript writing (Introduction, Methodology, Part of the result section, Discussion).

All authors read and approved the final manuscript

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