

Evaluating the relationship of gender with cardiovascular disease in non-diabetic subjects without micro and macro vascular complications

¹ *Geetha Bhaktha, ² Shivananda Nayak,
³ Manjula Shantaram, ⁴ Shreemathi Mayya

¹Research Scientist- II, Multidisciplinary Research Unit, Shimoga Institute of Medical Science, Shimoga, Karnataka, India.

²Department of Biochemistry, Subbaiah Institute of Medical Science, Shimoga, Karnataka, India.

³Department of Biochemistry, PG Centre, Chikka Aluvara, Somwarpet Taluk, Kodagu District, Mangalore University, Karnataka, India

⁴Department of Statistics, Manipal University, Manipal, Karnataka, India.

(*Corresponding Author)

Abstract

Aim: To study the Framingham cardiovascular risk assessment scores in male and female subjects without micro and macro vascular complications.

Materials and Methods: This study enrolled with 205 subjects without diabetes. All the subjects were without micro and macro vascular complications and were between 30-70 years of age. The Framingham cardiovascular risk scores were calculated for all the subjects. The scores were classified as Low: <10%, Moderate: 10-20% and High: > 20%

Results: Out of the 205 subjects, 162 (79%) subjects had a low risk, 27(13.2%) had a moderate risk and 16(7.8%) had a high risk of developing CVD in 10 years. Also females had a low risk of developing CVD than the males in low, moderate and high risk categorization.

Conclusion: The results of the study have fueled the ongoing debate on gender differences in developing CVD. Framingham risk scoring is a global risk assessment tool to predict the 10-year risk of developing CVD. The importance of prevention of micro vascular complications with appropriate glycemic control shows satisfactory benefits. Those subjects with high CVD scores should be followed up more regularly and treated effectively.

Key words: Cardiovascular disease, gender difference, risk.

INTRODUCTION

Leading cause of death is now considered to be cardiovascular disease, among which atherosclerotic cardiovascular disease is most notable. Gupta *et al.*, in their study reported that 25% of deaths are cardiovascular-related and would raise to more than 50% within next 15 years in India (1).

Both men and women have the same risk factor, but there are gender differences in the prevalence of risk factors. It is an illusion that females are less prone to coronary artery disease (CAD), incidences in their fertile age is less, though menopause age shows an increased prevalence of CAD. It is observed that a difference based on gender with respect to age of presentation exists. Therefore, diagnosis of CAD needs to be better understood by the treating physician so that appropriate and timely management can be specified. It is an observed fact that females consume an excess of fat and carbohydrates, do not exercise regularly and further, do not have much time to rest.

Over weight individuals especially with central fat deposition have been shown to be at increased risk of CVD mortality and morbidity (2), hence a universal risk factor for CVD (3). This may be associated with other risk factors like hypertension, dyslipidemia, diabetes collectively increasing the CVD events (4).

Apple type obesity and metabolic syndrome are independent risk factors for CAD mortality, more in women than men. A study by Bass *et al* has shown the indicator of CAD in both gender to be a decreased in HDL with elevated triglyceride and lipoprotein A(5).

It is therefore important for persons to be able to spot their own risks and susceptibility by having acquired knowledge (6). Moreover, very too little data are available in evaluating the predictive value of FRS in sensing the risk of CVD in subjects without any vascular disease

MATERIALS AND METHODS

This was a cross sectional study conducted in Dakshina Kannada district of Karnataka, India with 205 healthy individuals. The subjects aged between 30-70 years (both genders) were recruited for the study. The inclusion criteria for the subjects must be free from any pre existing cardiovascular disease, non-pregnant females and females free from usage of any hormones or oral contraceptives.

FBS was estimated by Glucose oxidase-peroxidase method. Lipid profile was measured using Agappe commercial kits. Total cholesterol was estimated by cholesterol-oxidase-peroxidase end point method, direct determination of HDL was done by immune inhibition end point method, triglyceride was estimated using GPO-PAP method. VLDL was calculated using the formula $VLDL = TG/5$. LDL was calculated by Friedwald's formulae ($LDL = VLDL + TG/5$).

HbA1c was measured by immune turbidometric technique. Spot urine sample was collected in a sterilized container and Microalbumin was estimated along with creatinine.

Clinical examination of pulse beats/minute, blood pressure, stress test (TMT) were measured for the assessment of cardiovascular system. Neuropathy, retinopathy and nephropathy were ruled out with relevant examination.

Cardiac stress test (or cardiac diagnostic test) was used to rule out any pre-existing CVD. Here the stress response is induced by exercise. Walking on a treadmill, any diagnosis of CVD, would rule out the criteria as a subject of the study.

Filament test and Quantitative sensory tests (QSTs) are techniques employed to rule out neuropathy. Fundoscopy was done to rule out retinopathy. Microalbuminuria test was used to rule out nephropathy

The study protocol was approved by the Ethics Committee of the Yenepoya University, Mangalore. Written informed consent was obtained from the selected subjects. Fasting blood sample of 5.0 ml was drawn to analyze FBS, lipid profile. Blood pressure was also measured with a gap of 5 minutes and their treatment for it was noted.

Anthropometric variables like WC, HC, height and weight were measured as per the standard procedure. Measurements of the weight to the nearest 0.1 kg by a weighing machine and height to the nearest of 0.1 cm by an anthropometer rod were done. BMI was calculated as weight (kg)/height (m²).

FRAMINGHAM RISK SCORE

Risk scores were calculated for only the CVD-unaffected individuals in our study. The cardiovascular risks of all subjects were determined using the Framingham risk scoring system according to the age, gender, systolic blood pressure, serum total and HDL cholesterol levels, smoking and hypertension treatment of subjects and presence of diabetes(7). According to the Framingham cardiovascular disease risk score; the 10-yr risk of CVD was classified as low (<10%), moderate (10 to 20%), or high (>20%)(8)

STATISTICAL ANALYSES

Data were presented as the mean \pm standard deviation. Baseline characteristics of the healthy subjects were tabulated and used to assess FRS. Based on the results, comparison between the male and female gender using the independent t-test was performed. The $P < 0.05$ was considered to indicate a statistically significant difference. Statistical analysis was performed using SPSS 10.0

RESULTS AND DISCUSSION:

The present study shows the Framingham risk score among healthy subjects with no vascular complication. The subjects had an overall good knowledge of CVD with good health promoting behaviors. Though most of the subjects in our study population(**Table 1**) were in low risk group, females were in a complete low risk category in contrast to men.

Table 1: Categorization of the study population based on FRS.

	Low	Moderate	High
Male(94)	51	27	16
Female(111)	111	-	-
Total(205)	162(79%)	27(13.2%)	16(7.8%)

Gender gap is a basic biological cause, which plays a key role in maintenance of homeostasis and causes exposure to cardio-metabolic risk factors, along with an expression of clinical picture and management of its associated features.

It is well recognized that numerous physiologic differences exist in men and women with not merely in baseline cardiac parameters, but also in the clinical presentation of it. Based on our study, it was able to show a statistical difference in anthropometric variables while other cardiovascular parameters did not clearly define the difference (**Table 2**).

Table 2: Gender specific characteristics of the study population

Parameters	Females(n=111)	Males(n=94)	P value
Age(years)	46.3±9.07	44.83±8.7	0.22*
Height in cm	156.5±7.35	165.18±7.3	0.0001***
Weight in kg	67.0±8.7	71.9±6.7	0.0001***
HC in cm	96.18±6.6	88.9±3.7	0.0001***
WC in cm	91.19±6.2	89.6±3.7	0.0326**
SP(mm Hg)	125.9±10.6	125.0±8.48	0.504 ^{NS}
DP(mm Hg)	92.65±9.29	89.8±6.65	0.015**
BMI(kg/m ²)	27.78±3.9	26.4±2.5	0.0025**
FBS (mg/dl)	78.07±12.8	77.1±13.8	0.6048 ^{NS}
PPBS(mg/dl)	105.0±10.6	105.7±9.6	0.6205 ^{NS}
Cholesterol(mg/dl)	191.4±19.1	193.5±22.9	0.4815 ^{NS}
HDL(mg/dl)	41.6±5.8	41.8±5.6	0.802 ^{NS}
LDL(mg/dl)	124.4±21.5	124.7±21.2	0.92 ^{NS}
VLD L(mg/dl)	25.4±5.4	26.9±5.6	0.053 ^{NS}
TG(mg/dl)	127.1±27.2	134.3±27.9	0.064 ^{NS}
hs-CRP(mg/dl)	0.13±0.07	0.13±0.09	1.00 ^{NS}
TNF- α (pg/ml)	12.33±7.07	10.38±9.10	0.0926 ^{NS}
Adiponectin(pg/ml)	17.9±9.3	18.4±7.4	0.6687 ^{NS}
Leptin(pg/ml)	9.0±5.7	7.5±3.8	0.0258**

*Significant; **Moderately significant; *** Highly significant; NS= Not significant

Reproductive factor and sexual function in women tend to develop heart disease later in life than men, signifying the attributed loss of estrogen through the menopausal transition; albeit, the component of cardio protection is exclusively due to reproductive hormones. Because of gender disparity, males though free from vascular complication were categorically available in the 3 groups. This study suggests that reproductive hormones offer meaningful protection for women from CVD than men. It is observed that the most major cause of death among women in the developed countries is Coronary Artery Disease which accounts for 30 % of it(9,10), the loss of estrogen sensitivity is observed as age advances, especially in the abdominal adipose tissues, which are the features of reminiscent metabolic syndrome(11). In our study all females were in the reproducible range and hence had a lower FRS than men (**Figure 1**) which was also seen in a study by damkonda *et al.*,(12).

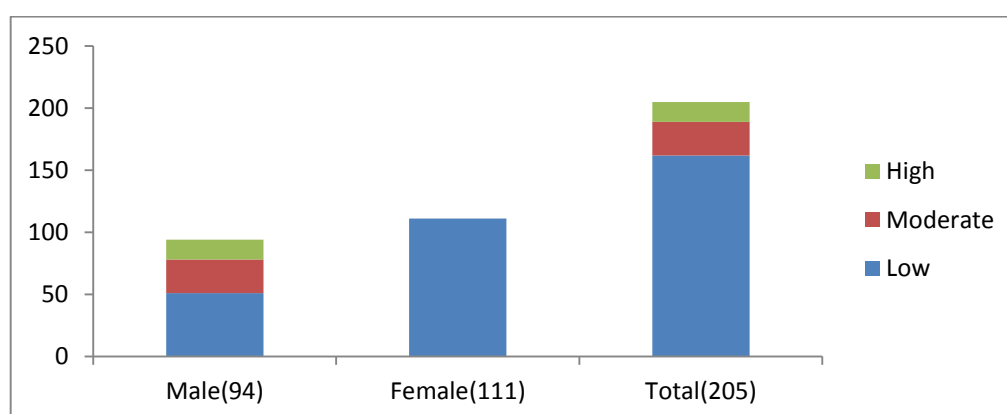


Figure 1: Cardiovascular risk stratification of participant according to FRS

The protective effect on CAD with regard to gender might be due to endogenous sex hormones like estrogen, progesterone along with androgens. It is an observed fact that these hormones have a major influence on the atherosclerotic processes (13). In females, the endogenous hormone estrogen protects against CAD in pre menopausal state but in post menopausal state when being supplemented.

But when used with hormone replacement therapy its net benefit in controlling CVD is considered to be less by American Heart Association(14). It has been suggested that the premenopausal women are at low risk implying the positive effect of female hormones on vascular activity, lipid profile, endothelial function, or other cardio protective substances(15,16)

A steady increase in adiposity in the course of life seems to induce the relationship between leptin and adiponectin, which is more obvious in women than in men(17). It is observed that serum adiponectin levels decrease, with an increase in circulating leptin levels with respect to body fat mass. In our study, (**Table 2**) though females had a lower adiponectin concentration, it was not statistically significant. But the leptin levels were higher in females and the difference in leptin concentration between the gender was statistically significant.

The prevention and diagnosis of CVD in men and women are clinically disputable. The risk factor that Women face during pregnancy, menopause, polycystic ovarian syndrome and connective tissue diseases is often over looked. Hence tools to quantify the risk and its interventions to decrease is much needed.

Observation and information about CVD and its modifiable factors is a crucial step to change the people's wellbeing states of life (18,19). Hence good knowledge about modifiable risk factors for CVD risk is of paramount importance. (20, 21)

CONCLUSION

Evidence suggests that FRS by itself is most useful tool for risk prediction, particularly when they have multiple modifiable risks. Adjustments in these risk factors improve the occurrence of CVD and show adequate benefits. Hence decrease the burden associated with CVD.

ACKNOWLEDGMENT:

We would like to express our gratitude to Dr. G.S. Chandrashekar, Senior Physician and Cardio Diabetologist of Adarsha Hospital and Institute of Cardio Diabetes, Trauma & Joint Replacement, Udupi, Karnataka for his support in conducting this study.

REFERENCES

- [1] Gupta, R., Joshi. P., Mohan. V., Reddy, K.S., Yusuf, S.,2008,"Epidemiology and causation of coronary heart disease and stroke in India. Heart" 94, pp.16-26.
- [2] Van Gaal, L.F., Mertens, I.L., De Block, C.E.,2006 "Mechanisms linking obesity with cardiovascular disease", Nature.,444, pp.875–880.
- [3] Din-Dzietham, R., Liu ,Y., Bielo M.V., et al.,2007, "High blood pressure trends in children and adolescents in national Surveys, 1963 to 2002", Circulation, 116(13), pp.1488–96
- [4] Ritchie, S.A., Connell, J.M.,2007 "The link between abdominal obesity, metabolic syndrome and cardiovascular disease",Nutr Metab Cardiovasc Dis.,17(4), pp.319–26.
- [5] Bass, K.M., Newschaffer, C.J., Klag, M.J., Bush, T.L.,1993 "Plasma lipoprotein levels as predictors of cardiovascular death in women", Arch Intern Med,153 , pp. 2209-16.
- [6] Deaton, C., Froelicher, E. S., Wu, L. H., Ho, C., Shishani, K., Jaarsma, T,2011, "The global burden of cardiovascular disease",European Journal of Cardiovascular Nursing,10(Suppl. 2), S5eS13.
- [7] Framingham Heart Study: General cardiovascular disease (10 years risk): risk

- score calculators. [Online]
- [8] Murphy, T.P., Dhangana, R., Pencina, M.J., Zafar, A.M., D'Agostino, R.B., 2011 "Performance of current guidelines for coronary heart disease prevention: optimal use of the Framingham-based risk assessment", *Atherosclerosis*, 216 , pp.452-7.
 - [9] Lerner, D.J., Kannel, W.B., 1986 "Patterns of coronary heart disease morbidity and mortality in the sexes: a 26-year follow-up of the Framingham population", *Am Heart J*, 3 , pp.393–390.
 - [10] National Center for Health Statistics. 1988 Vital statistics of the United States 1986. II. Mortality, A and B. Washington DC: US Department of Health and Human Services; publications 88–1122 and 88–1113.
 - [11] MC, Carr. 2003, "The emergence of the metabolic syndrome with menopause", *J Endocrinol Metab.* 88 , pp.2404-2411.
 - [12] Damkondwar, D.R., Raman, R., Suganeswari, G., Kulothungan, V., Sharma, T., 2012 "Assessing Framingham cardiovascular risk scores in subjects with diabetes and their correlation with diabetic retinopathy", *Indian J Ophthalmol.*, 60 , pp.45–8.
 - [13] Hanes, D.S., Weir, M.R., Sowers, J.R., 1996 "Gender considerations in hypertension pathophysiology and treatment", *Am J Med.* 101 , pp.10S–21S.
 - [14] Mosca, L., Benjamin, E.J., Berra, K., et al. 2011, "Effectiveness-based guidelines for the prevention of cardiovascular disease in women--2011 update: a guideline from the American heart association" *Circulation*, 123(11), pp.1243-1262.
 - [15] Coutinho, T., 2014, "Arterial stiffness and its clinical implications in women", *Can J Cardiol.*, 30(7), pp.756-764.
 - [16] Chou, A.Y., Saw, J., 2014 "Basis for sex-specific expression of Takotsubo cardiomyopathy, cardiac syndrome X, and spontaneous coronary artery dissection", *Can J Cardiol.*, 30(7) , pp.738-746.
 - [17] Lecke, S.B., Morsch, D.M., P.M., 2011, "Spritzer .Leptin and adiponectin in the female life course", *Braz J Med Biol Res*, 44(5) , pp.381-387.
 - [18] Becker, M.H., Maiman, L.A., Kirscht, J.P., Haefner, D.P., Drachman, R.H., 1977 "The Health Belief Model and prediction of dietary compliance: a field experiment", *J Health Soc Behav*, 18 , pp.348–366.
 - [19] Ford, E.S., Jones, D.H., 1991 "Cardiovascular health knowledge in the United States: findings from the National Health Interview Survey, 1985", *Prev Med*, 20 , pp.725–736.
 - [20] European Guidelines on cardiovascular disease prevention in clinical practice (version 2012). The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by r. Perk J, De Backer G, Gohlke H, Graham I, Reiner Z, Verschuren WM, Albus C, Benlian P, Boysen G, Cifkova R, Deaton C, Ebrahim S, Fisher M, Germanò G, Hobbs R, Hoes A, Karadeniz S,

Mezzani A, Prescott E, Ryden L, Scherer M, Syvanne M, Scholte Op Reimer WJ,.

- [21] Al Hamarneh, Y.N., Crealey, G.E., McElnay, J.C.,2011, “Coronary heart disease: health knowledge and behavior”, *Int J Clin Pharm*, 33 , pp.111–123.