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**Title: To stratify the risk of having coronary heart disease in postmenopausal women using Framingham scale in Eastern Nepal**

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**ABSTRACT**

**Introduction:** Cardiovascular disease (CVD) is one of the leading causes of mortality and morbidity in both developed and developing countries. CVD risk rises to double fold in women after menopause. We aim to stratify menopausal women of our region for having coronary heart disease in next 10 years.

**Methods:** One year cross sectional study was conducted in General Out Patient Department (GOPD) of a tertiary care center of eastern Nepal. The Standard ATP calculator was used and the relevant necessary data was introduced into the calculator and the automated result was collected.

**Results:** Among 272 participants above fifty percent had Framingham score 1-5%. And the risk was greater within first five years after menopause in 50-59 years of age group. Similarly, with advancing age and longer duration of menopause the risk became significantly higher.

**Conclusion:** Besides the established risk factors for CVD, postmenopausal state is additional risk for women and this study emphasizes this factor as risk of CVD even in our set up.

**Key words:** Cardiovascular Disease, Menopause, Framingham score, Postmenopausal women.

**INTRODUCTION**

Cardiovascular disease (CVD) has been the leading cause of mortality and morbidity of both men and women in developed as well as developing countries. CVD refer to disease affecting blood vessels and heart; and usually atherosclerosis associated.1Atherosclerotic plaques are thickened intima with various mixtures of fibrous tissues, cells, and lipid deposition with chronic inflammation.2, 3,4CVD risk factors are categorized into major independent risk factors and predisposing factors including several lifestyle variables and laboratory parameters.5The incidence and prevalence of coronary artery disease varies with the life cycle of women. The risk is lower in premenopausal state and increases in postmenopausal state. The offspring’s of Framingham heart study who were gynecologically normal, and were not taking any hormones showed that menopause is positively correlated with LDL cholesterol and decreased LDL particle size.6CVD accounts for one third of all deaths and the rate is even higher for South Asian women.7

In country like Nepal, elderly women are under privileged, less literate, less health aware and health professionals are weakly concerned of advancing cardiovascular risk in this age group. American Heart Association (AHA) survey reveals that many (38%) women underestimate the importance of CVD risk and that this issue is not often discussed. This looses the opportunity to prevent CVD mortality and morbidity by lifestyle modifications.8Our study sets out to identify the risk score using Framingham risk assessment tool to predict the chance of having coronary heart disease in next 10 years. Here the subjects will get a chance to look at their future risk of developing coronary heart disease and the chance for timely intervention like life style modification and therapeutic intervention to prevent cardiovascular event.

**METHODS**

This was a yearlong observational study conducted in General Out Patient Department of tertiary care center of eastern Nepal. With permission from ethical clearance board and with informed consent, postmenopausal women were interviewed. Post-menopause for this study purpose was defined as cessation of menstruation naturally for at least one year. Exclusion criteria were previously diagnosed heart disease, past history of stroke or transient ischemic attack. Individuals meeting the criteria were interviewed using a semi standardized Performa. Blood pressure was assessed one time at the right upper arm after a 5 min rest in the sitting position with a manual mercury sphygmomanometer. Biomedical tests (Fasting Total Cholesterol, High Density Lipoprotein-Cholesterol, and Fasting Blood Sugar) was done using a fasting venous blood sample after 12-hr fast at the central laboratory on a voluntary fee pay basis and reports were collected on patient's follow up visits. Framingham score was calculated using the download version ATP Risk Estimator .xlsm 12001 updated. The relationship between age, duration of menopause in years smoking habit were cross tabulated with Framingham score, where Framingham score was the dependent variable. The results was classified as follows: Low risk- Less than 10% chance, Intermediate risk- 10%-20% chance, High risk- more than 20% chance. All the data as recorded in the Performa was entered into the Excel database was analyzed by the SPSS-17 program (Chicago, IL, USA).

**RESULTS**

This study included 272 post menopausal patients from July 2011 through June 2012 who presented with complaints other than cardiac. The age ranged from youngest 50years to oldest 80years. The duration of menopause ranged from 1-26years.The most common age to present in decades was in 6th decades (n=151) followed by 7th decades (n=83)(Table1)

**Table 1: Physical and clinical characteristics of subjects (n=272)**

|  |  |
| --- | --- |
| Characteristics | Mean(SD) |
| Age (in years) | 60.34(7.322) |
| Age of menopause (in years) | 7.24(6.313) |
| Systolic blood pressure (mmHg) | 127.92(15.680) |
| Total Cholesterol (mg/dl) | 178.55(44.165) |
| HDL (mg/dl) | 38.38(3.819) |
| Framingham 10 years risk estimation | 4.283 |

**Table 2. Variables of participants**

|  |  |  |
| --- | --- | --- |
| Variables  | Frequency | Percent |
| Age in decades | 50-59 | 151 | 55.5 |
| 60-69 | 83 | 30.5 |
| 70-79 | 35 | 12.9 |
| 80-89 | 3 | 1.1 |
| Duration of Menopause in Years (DMY) | 1-5 | 147 | 54.0 |
| 6-10 | 51 | 18.8 |
| 11-15 | 35 | 12.9 |
| 16-20 | 29 | 10.7 |
| 21-25 | 10 | 3.7 |
| Religion | Buddhist | 12 | 4.4 |
| Christian | 24 | 8.8 |
| Hindu | 212 | 77.9 |
| Kirat | 24 | 8.8 |
| Education | Illiterate  | 147 | 54 |
| Primary | 85 | 31.3 |
| Secondary | 24 | 8.8 |
| Higher | 16 | 5.9 |
| Occupation | Home maker | 118 | 43.4 |
| Farmer  | 74 | 27.7 |
| Business | 34 | 12.5 |
| Employed | 13 | 4.8 |
| Pension | 33 | 12.1 |
| Diet | Non-vegeterian | 249 | 91.5 |
| Vegeterian | 23 | 8.5 |
| Smoking  | Yes  | 194 | 71.3 |
| No  | 78 | 28.7 |
| Duration of exercise | Less than 150min/week | 12 | 4.4 |
| More than 150min/week | 5 | 1.8 |
| No exercise | 255 | 93.8 |
| Weight in Kgs | 40-49 | 28 | 10.3 |
| 50-59 | 151 | 55.5 |
| 60-69 | 63 | 23.2 |
| 70-79 | 26 | 9.6 |
| 80-89 | 4 | 1.5 |
| Waist in Cms | 60-69 | 23 | 8.5 |
| 70-79 | 154 | 56.6 |
| 80-89 | 72 | 26.5 |
| 90-99 | 18 | 6.6 |
| 100-109 | 5 | 1.8 |

This study showed 5.5% (n=15) had total cholesterol(TC) below 120mg/dl, 75.36% (n=205) had between 121-210mg/dl and 19.11% (n=52) had above 211mg/dl. Within first 5years of menopause 90 subjects had HDL-C <39 and the occurrence gradually decreased with the increase in DMY whereas those having HDL-C>50 didn’t gradually increase with increase in DMY (Table 3).

**Table 3: Relation between Duration of Menopause and total cholesterol and HDL-C**

|  |  |  |  |
| --- | --- | --- | --- |
| Lipid profile | Values in mg/dl | DMY (years) | p-value |
| **1 to 5** | **6 to 10** | **11 to 15** | **16 to 20** | **21 to 25** |
| Total cholesterol | <120 | 5 | 3 | 3 | 2 | 2 | 0.258 |
| 121-210 | 109 | 40 | 28 | 23 | 5 |
| >211 | 33 | 8 | 4 | 4 | 3 |
| Total | 147 | 51 | 35 | 29 | 10 |
| HDL | <39 | 90 | 24 | 22 | 21 | 6 | 0.260 |
|  40-49 | 56 | 27 | 13 | 7 | 4 |
| >50 | 1 | 0 | 0 | 1 | 0 |
| Total | 147 | 51 | 35 | 29 | 10 |

Similar pattern was recorded with age. Here 50% of the study population had SBP between 121-139mmHg and the result was not statistically significant with DMY and age.(Table 4)

Among total subjects, n=90, (30.73%) were diabetic and n=75 had low risk, n=14 had intermediate risk and n=1 had high risk score and the result was statistically significant.

**Chart 1: Distribution of 10 Yrs CHD Risk Score (Framingham Score)**

For Framingham score distribution, 89.7% of women had low risk (<10%), 9.9% had intermediate risk (10-20%) and 0.4% had high risk (>20%) of 10 yrs CHD risk. Similarly the occurrence of risk score was high in 50-59years of life followed by 60-69years and then 70-79years. A significant number (n=11) out of 27 of intermediate score were70-79years followed by n=7 were 50-69 years.(Chart 1)

With increase in duration of menopause, the Low risk (<10%) occurrence gradually decreased whereas the occurrence of High risk (>20%) didn’t increase in ascending order. From intermediate score group (N=27), n=9 had the longest duration of menopause (20-25years) (Table 4)

**Table 4: Relation between DMY, Total cholesterol, HDL-C &Framingham score**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Variables | Low (<10%) | Intermediate (10-20%) | High (>20%) | p-value |
| DMY(Years) | 1-5 | 140 | 7 | 0 | **˂0.001** |
| 6-10 | 47 | 4 | 0 |
| 11-15 | 31 | 3 | 1 |
| 16-20 | 25 | 4 | 0 |
| 21-25 | 1 | 9 | 0 |
| **Total** | **244** | **27** | **1** |
| Total Cholesterol (mg/dl) | <120 | 14 | 1 | 0 | **˂0.001** |
| 121-210 | 194 | 11 | 0 |
| >211 | 36 | 15 | 1 |
| **Total** | **244** | **27** | **1** |
| HDL-C(mg/dl) | <39 | 44 | 18 | 1 | 0.741 |
| 40-49 | 98 | 9 | 0 |
| >50 | 2 | 0 | 0 |
| **Total** | **244** | **27** | **1** |

The cross tabulation of TC and Framingham score showed statically significant result with n=205 having TC 121-210mg/dL and n=52 having >211mg/dL and one subject from this group had high risk score.(Table 6) The cross tabulation between HDL-C and Framingham score was not statically significant. Among t=272, n=163 had HDL-C <39 and n=1(t=163) had high risk score.(Table 4)

**DISCUSSION**

Several studies on increasing cardiovascular risk in post-menopausal women put insight in importance of early screening and timely intervention for primary prevention. Here in this study Framingham Risk assessment tool has been used to calculate the 10years CHD risk and traditional CVD risk factors have been assessed. Among 272subjects, more than three quarters n= 244 subjects (89.7%), had projected 10 years risk of CHD risk <10%. The outcome was quite different in a comparative study with total 691 subjects aged 30-70 years , n=59 subjects (8.5%) had projected 10 year coronary heart disease risks > 30%, and 291 (42.1%) had risks > 15%.9

The mean Framingham risk estimation of participants in this study was 4.28 which are comparable with a study done on Iranian postmenopausal women with mean risk 1.46. The estimated 10 years risk for CHD was greater in this study, which could be because the mean age of the participants was high (mean age =60.34years) and it has adopted the calculator from the original Framingham study but the performance of the scale in Asian population is not clear.10This study illustrates 20% of study population had TC >211mg/dL and the occurrence (n=146) of TC>121mg/dL was in age group 50-59 years. The highest number of subjects(n=142) developed this after 1-5years of menopause and this was 54% rise in CHD risk and was found to decline gradually in the following ages. A study by Mathews et al. in SWAN (Study of Women's Health across the Nation), discussed that total cholesterol, LDL-C, HDL-C changes with menopause in first 1 year. And several studies also have shown a strong positive relationship of total cholesterol (TC) above 180mg/dl with CHD risk and death.11,12

On the basis of those studies, the rise in CHD risk in first few years of menopause is implacable to the postmenopausal women of this study group. And this issue is addressed by ATPIII of the National Cholesterol Education Program (NCEP) guideline which suggests that if one's FRE is <10% with 2+ risk factors, one's LDL goal should be <130, and individuals with FRE <10% with 0 to 1 risk factors should have a LDL goal of <160.

Similarly, several other studies have established a powerful protective inverse relation between increasing HDL and incidence of CHD. Low HDL concentrations less than 40mg/dl have a greater risk for CHD.13 In this study, 59.92% (n=163) (total n=272) of participants had HDL less than 39, among this (n=92) had 10years CHD risk between 1-5%. Who had menopause within last 1-5 years (n=90) had HDL <39mg/dL. This result is comparable with the result from a study done on Iranian postmenopausal women which showed only 22.4% of participants with HDL less than 40. This indicates that the women from our region are at higher risk for CHD than Iranian women.

**CONCLUSION**

The Framingham risk was comparatively greater within first five years after menopause in 50-59years of age group. With advancing age and longer duration of menopause the Framingham risk became gradually higher. So, postmenopausal state is an additional risk for CVD in women even in our set up.

**REFERENCES**

1. The medical news. What is cardiovascular disease? [Online]. 2011 [cited 2011 Jan 25]; Available from: URL: <http://www.news-medical.net/health/What-is-Cardiovascular-Disease.aspx>

2. Tabas I., Williams KJ, Boren J. Sub endothelial lipoprotein retention as the initiating process in atherosclerosis: update and therapeutic implications. Circulation. 2007;116:1832–44. DOI: <https://doi.org/10.1161/CIRCULATIONAHA.106.676890>PMid:17938300

3. Witztum JL. The role of oxidized LDL in the atherogenic process. J Atheroscler Thromb 1994;1:71–5. DOI: <https://doi.org/10.5551/jat1994.1.71>PMid:9222872

 4. Barrett-Connor E. Heart disease in women. Fertil Steril. 1994;62 [Suppl. 2]:127S–32S.PMid:7958006

 5. Grundy SM, Pasternak R, Greenland P, Smith S, Fuster V. Assessment of Cardiovascular Risk by Use of Multiple-Risk-Factor Assessment Equations. A Statement for Healthcare Professionals from the American Heart Association and the American College of Cardiology. J Am Coll Cardiol. 1999;34:1348 –59. DOI: [https://doi.org/10.1016/S0735-1097(99)00387-3](https://doi.org/10.1016/S0735-1097%2899%2900387-3)

6. Manson JW, Spelsberg A. Risk modification in the diabetic patient. In: Manson JE, Ridker PM, Gaziano JM, et al, eds. Prevention of Myocardial Infarction. New York: Oxford University Press, Inc., 1996:241–273.

7. Jackson G. Coronary artery disease and women. BMJ: British Medical Journal. 1994 Sep 3;309(6954):555. DOI: <https://doi.org/10.1136/bmj.309.6954.555>PMid:8086940 PMCid:PMC2541423

 8. Wikipedia. [Online]. 2011 [cited 2011 Jan 25]; Available from: URL: http://en.wikipedia.org/ wiki/Nepal

 9. Jones AF, Walker J, Jewkes C, Game FL, Bartlett WA, Marshall T, Bayly GR. Comparative accuracy of cardiovascular risk prediction methods in primary care patients. Heart 2001;85:37–43. DOI: <https://doi.org/10.1136/heart.85.1.37>PMid:11119458 PMCid:PMC1729574

 10. D'Agostino RB, Russell MW, Huse DM, et al. Primary and subsequent coronary risk appraisal: new results from The Framingham Study. Am Heart J. 2000;139:272–81. DOI: <https://doi.org/10.1067/mhj.2000.96469>, [https://doi.org/10.1016/S0002-8703(00)90236-9](https://doi.org/10.1016/S0002-8703%2800%2990236-9)

 11. Matthews KA, Crawford SL, Chae CU, et al. Are changes in cardiovascular disease risk factors in midlife women due to chronological aging or to the menopausal transition? J Am Coll Cardiol. 2009 Dec 15;54(25):2366-73. DOI: <https://doi.org/10.1016/j.jacc.2009.10.009>PMid:20082925 PMCid:PMC2856606

12. Neaton JD, Blackburn H, Jacobs D, Kuller L, Lee DJ, Sherwin R, et al. Serum cholesterol level and mortality findings for men screened in the multiple risk factor intervention trial. Multiple risk factor intervention trial research group. Arch Intern Med. 1992;152(7):1490-1500. DOI: <https://doi.org/10.1001/archinte.1992.00400190110021>, <https://doi.org/10.1001/archinte.152.7.1490>PMid:1627030

 13. MRC/BHF heart protection study of cholesterol lowering in 20536 high risk individuals: a randomized controlled clinical trial. Heart Protection Study Collaborative Group. Lancet 2002;360(9326):7-22. DOI: [https://doi.org/10.1016/S0140-6736(02)09327-3](https://doi.org/10.1016/S0140-6736%2802%2909327-3)