FRAMINGHAM RISK SCORE IN ESTIMATING CARDIOVASCULAR DISEASE RISK FACTORS IN PEOPLE OF ASIAN INDIAN ORIGIN: A STUDY ON RURAL ADULT POPULATION IN WEST BENGAL, INDIA

Tanmay Nag and Arnab Ghosh*

Biomedical Research Laboratory, Department of Anthropology, Visva Bharati University, Santiniketan, West Bengal, India.

*Author for Correspondence: Dr. Arnab Ghosh
Biomedical Research Laboratory, Department of Anthropology, Visva Bharati University, Santiniketan, West Bengal, India.
arnab_cu@rediffmail.com

ABSTRACT
Aims: This study was aimed to investigate the efficacy of Framingham risk score (FRS) in estimating cardiovascular disease (CVD) risk in a rural adult population in West Bengal, India. Methods: This cross-sectional study was carried out among 1007 participants (645 males and 362 females) aged 20 to 80 years in a rural adult population in West Bengal, India. Anthropometric measures and blood pressure were collected using standard techniques. Metabolic profiles and insulin was also estimated and HOMA-IR was calculated subsequently. Results: The higher mean was observed for age, height, waist circumference, waist-hip ratio, total cholesterol, triglycerides, low and very low density lipoprotein cholesterol, fasting blood glucose, systolic and diastolic blood pressure and mean arterial pressure with increasing FRS category. On the contrary, lower mean was found for weight, hip circumference, waist-to-hip ratio, body mass index, percentage body fat, sum of four skinfolds, high density lipoprotein cholesterol, insulin and insulin resistance. Significant age group difference was found in respect to FRS category. No remarkable difference was noticed in the prevalence of metabolic syndrome with increasing FRS. Conclusion: More comprehensive risk prediction algorithm is required to better comprehend the CVD and its' risk factors in this population.

KEYWORDS: FRS, CVD, type 2 diabetes, metabolic syndrome, Asian Indians.

INTRODUCTION
Cardiovascular disease (CVD) is the number one cause of death in the world.[1] The prevalence of CVD is increasing worldwide and it accounts for 17% of the total mortality.[2] It is presumed that not only developed countries will be affected by CVD, the developing countries will also equally, even more, will be affected.[3] It has been predicted that by the year 2020, there will be an increase by almost 75% in global CVD prevalence, and almost all of these increases will occur in developing countries.[4] It has been predicted that by 2030, almost 23.6 million people will die from CVD, mainly from heart disease and stroke.[5]

It has been estimated that by 2020, CVD will be the largest cause of disability and death in India, with 2.6 million Indians predicted to die due to CVD.[6, 7] It has been predicted that by the year 2020 there will be a 111% increase in CVD deaths in India. It has also been predicted that India would be the heart disease capital in the world by 2020.[8] By 2020, 2.6 million Indians are predicted to die due to coronary heart disease (CHD), which constitutes 54.1% of all CVD deaths.[9,10] Several surveys conducted across the country have shown a rising prevalence of major risk factors for CVD in urban as well as rural population.[11, 12] It was seen in a survey conducted in 45 rural villages in India, 32 per cent of all deaths were due to CVD. On the other hand, infectious diseases were responsible for 13 per cent. It proves that the epidemic has reached its advanced stage even in rural India.[13]

To date, many CVD risk assessment tools have been devised.[14] The Framingham risk score (FRS) originated from the Framingham Heart Study (FHS), a relatively homogeneous cohort residing in Framingham, Massachusetts,[15] and has been applied and validated in a variety of different populations.[16, 17] The FRS is most widely used by clinicians across the globe.[18] FRS has traditionally been used as a predictor of the 10-year risk of CHD.[19] The FRS is an extensively studied index to predict CVD risk in the general population.[20] It includes age, gender, smoking, blood pressure and cholesterol concentrations and estimates the 10-year risk of coronary events by
stratifying individuals into three risk categories: low (<10%), intermediate (10% - 20%) and high (>20%).[22]

Metabolic syndrome (MS), which is a clustering of atherogenic metabolic abnormalities, has emerged as an important determinant of CVD risk.[23, 24] MS is associated with increased risk of developing type 2 diabetes mellitus (T2DM) as well as CVD in different ethnic populations. The MS, as a principal cause for diabetes and CVD, is considered as a major challenge to public health throughout the world. MS is associated with a doubling of the risk of CVD.[25] Individuals with MS have a 30%-40% probability of developing diabetes and/or CVD within 20 years, depending on the number of components present.[26]

It was observed that individuals with clustering of CVD risk factors i.e. individuals having more than one risk factor were more prone to develop CVD compared with those with a single CVD risk factor.[27] The co-occurrence of multiple risk factors increases the risk of CVD morbidity and mortality.[28-30] It was reported that 1 or more CVD risk factors were present in 85% to 90% of adults with CHD.[31-32] It was also reported that a decrease in the number of risk factors has been associated with a reduction in CVD risk.[33]

The efficacies of FRS have mostly been studied in industrial and particularly in urban Indian population and there is scant information on the efficacy of FRS in rural Asian Indian population. However, to the best of the authors’ knowledge, virtually no study has been undertaken on rural adult population in India to find out the efficacy of FRS in identifying the individuals with increased risk of developing CVD. Keeping this in mind, the present community-based cross-sectional study were undertaken to investigate the efficacy of FRS in identifying the individuals with increased risk of developing CVD among rural adult population in West Bengal, India.

SUBJECTS AND METHODS

Study population

This cross-sectional study was carried out between July 2012 and February 2014 in 1007 participants (645 males and 362 females) aged ≥ 20 years in a rural community. The participants were categorized by age groups as: 20-29 years (n = 79); 30-39 years (n = 140); 40-49 years (n = 272); 50-59 years (n = 347); and ≥ 60 years (n = 169). All individuals were recruited from the Bolpur-Santiniketan area [about 160 km from Kolkata (erstwhile Calcutta)] West Bengal, India. Women on hormone therapy, pregnant women as well as individuals suffering from chronic diseases (diagnosed) for example diabetes, hypertension, CVD, etc were not considered in the study. All the participants were explained the purpose of the study and were assured that the information would be kept strictly confidential. Only one subject was chosen from each household to avoid intra-household clustering of CVD risk factors. Written consent was taken from each individual prior to the actual commencement of the study. The institutional ethics committee of the ‘Human Genetic Engineering Research Centre’ (HGERC), Kolkata, India had approved the study.

Anthropometric and body composition measures

Anthropometric measures, such as, height, weight, circumferences of minimum waist (MWC) and maximum hip (MHC) as well as skinfold thickness at biceps (BSF), triceps (TSF), subscapular (SSSF) and suprailiac (SISF) were taken using standard techniques.[34] Height and weight were measured to the nearest 0.1 cm and 0.5 kg, respectively, with subjects wearing light cloths and without shoes. Waist and hip circumferences were measured with a non-stretchable tape to the nearest 0.1 cm. Skinfolds thicknesses were measured to the nearest 1 mm using a Holtain skinfold calliper (Holtain Corporation, UK). Percentage of body fat (% BF) and body mass index (BMI) were measured using Omron body fat analyzer (Omron Corporation, Tokyo, Japan). Waist-hip ratio (WHR), waist–height ratio (WHtR) and sum of four skinfold thickness (\( \sum S_{F_i} \)) were computed subsequently.

Blood pressure

Left arm systolic (SBP) and diastolic (DBP) blood pressure were taken from each participant in a sitting position using a standard mercury sphygmomanometer according to a standard protocol. The 1st and 5th Korotkoff sounds were recorded as SBP and DBP, respectively. Two blood pressure measurements were taken and averaged for analyses. A third measurement was taken when the difference between the two measurements was ≥ 5 mmHg, and a subsequent mean was calculated. A five minute relaxation period between measurements was allowed for all participants. Mean Arterial Pressure (MAP) was calculated subsequently using the standard formula: MAP = DBP + 1/3(SBP-DBP).

Metabolic profiles

A fasting blood sample (~7 ml) was collected from each individual for the determination of fasting blood glucose (FBG), total cholesterol (TC), triglyceride (TG) and high density lipoprotein (HDL). All individuals maintained an overnight fast of 10 to 12 hours prior to blood collection. The plasma was separated by centrifugation at 1000 rpm for 20 min at room temperature within 2 hours of collection. TC, TG, FBG and HDL were estimated on separated plasma using semi auto-analyzer (Mindray BA 88A, China). Low density lipoprotein (LDL) cholesterol and very low density lipoprotein (VLDL) cholesterol were then calculated by using the standard formula[35]: VLDL = TG/5 and LDL = TC - (HDL + VLDL). All metabolic variables were measured in mg/dl (mg %) unit. Serum insulin was estimated using chemiluminescent microparticle immuno assay

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(CMLA) method (ARCHITECT i2000 SR, ABBOTT, Germany) for the subjects (n = 101) with fasting glucose ≥ 100 mg %. Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) was then calculated by the following formula:\[36]

\[
\text{HOMA-IR} = \frac{\text{FBG (mg/dL) x fasting insulin (\muU/mL)}}{22.5}
\]

Framingham risk score (FRS)
The FRS was calculated taking into consideration the age, gender, smoking status, total cholesterol, HDL cholesterol and blood pressure.\[22\] It was found in the present study that there were only 6 participants in the high risk category. Hence, the study population were divided into 2 risk categories, such as, ‘low risk’ (<10%) (n = 784) and ‘intermediate to high risk’ (≥10%) (n = 223) by clubbing intermediate risk and high risk instead of 3 risk categories i.e. low risk (<10%), intermediate risk (10-20%) and high risk groups (>20%).\[20, 22\]

Metabolic syndrome (MS)
In the present study MS was defined according to consensus definition for adult Indians.\[37\] Participant was defined as having MS if the participant met three or more of the following five conditions: WC > 90 cm (male) and > 80 cm (female); TG ≥ 150 mg%; FBG ≥ 100 mg%; BP ≥ 130/ ≥ 85 mmHg; HDL < 40 mg% (male) and < 50 mg% (female).

Statistical analyses
Descriptive statistics such as mean and standard deviation (SD) of variables was calculated according to FRS category and ANOVA was executed to study the significant group differences of variables. Chi-square test was performed to find the relation of age groups in respect of FRS category. The prevalence (%) of MS phenotypes was computed by FRS category. The prevalence of CVD risk factors clustering was also compared by FRS category. All statistical analyses were carried out using the SPSS (PC+ version 14.0). A p value of < 0.05 was considered as significant.

RESULTS
Comparison of anthropometric measures, body compositions, lipid profiles, blood glucose, blood pressure and insulin according to FRS category is presented in Table 1. The higher mean (±SD) for age, height, MWC, WHR, TC, TG, LDL, VLDL, FBG, SBP, DBP and MAP and lower mean (±SD) for weight, MHC, WHR, BMI, %BF, \(\Sigma SF_4\), HDL, Insulin and HOMA-IR were found with increasing FRS category. Significant (p<0.05) differences were found for age, height, MWC, MHC, WHR, BMI, %BF, \(\Sigma SF_4\), TC, TG, HDL, LDL, VLDL, FBG, SBP and MAP in respect to FRS category, whereas, no significant differences were evident for weight, WHR, DBP, Insulin and HOMA-IR.

Chi-square test to observe the association between age-groups and FRS category is presented in Table 2. Significant (p<0.0001) age group differences were evident in according to FRS category.

Prevalence of MS phenotypes according to FRS category is presented in Table 3. Higher prevalence of high TG, high FBG and high BP was found with increasing FRS category. On contrary, lower prevalence of high WC and low HDL was evident with increasing FRS category. Moreover, no remarkable difference was observed in the prevalence of MS with increasing FRS category.

The prevalence of CVD risk factors clustering according to FRS category is presented in Figure 1. Higher prevalence of the clustering of (high TG & high FBG & high BP) (5.74% vs. 12.56%) and (high TC & high TG & high BP) (3.83% vs. 10.31%) was found with increasing FRS category.

Table 1: Comparison of anthropometric measures, body composition, lipid profiles, blood glucose, blood pressure and insulin by FRS category (n = 1007).

<table>
<thead>
<tr>
<th>Variables</th>
<th>FRS category</th>
<th>ANOVA</th>
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<tbody>
<tr>
<td></td>
<td>Low risk (n = 784)</td>
<td>Intermediate to high risk (n = 223)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>45.38±11.16</td>
<td>59.65±8.61</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>159.26±9.22</td>
<td>163.32±7.11</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>64.43±12.09</td>
<td>64.16±11.52</td>
</tr>
<tr>
<td>MWC (cm)</td>
<td>81.25±8.68</td>
<td>82.64±8.00</td>
</tr>
<tr>
<td>MHC (cm)</td>
<td>93.28±7.95</td>
<td>90.61±7.06</td>
</tr>
<tr>
<td>WHR</td>
<td>.86±.05</td>
<td>.90±.03</td>
</tr>
<tr>
<td>WHR</td>
<td>.51±.05</td>
<td>.50±.04</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.36±4.04</td>
<td>23.98±3.52</td>
</tr>
<tr>
<td>%BF</td>
<td>31.45±7.05</td>
<td>28.91±5.39</td>
</tr>
<tr>
<td>(\Sigma SF_4) (mm)</td>
<td>57.29±20.36</td>
<td>46.14±15.54</td>
</tr>
<tr>
<td>TC (mg%)</td>
<td>162.64±28.12</td>
<td>169.79±31.95</td>
</tr>
<tr>
<td>TG (mg%)</td>
<td>149.65±59.02</td>
<td>161.79±60.62</td>
</tr>
</tbody>
</table>
HDL (mg%) 47.17±7.38 45.46±6.94 0.002
LDL (mg%) 85.74±23.12 91.96±26.71 0.001
VLDL (mg%) 29.73±10.43 32.35±12.12 0.001
FBG (mg%) 90.93±27.34 98.29±32.46 0.001
SBP (mmHg) 124.65±17.17 136.34±19.25 <0.001
DBP (mmHg) 81.23±8.70 81.78±8.44 0.400
MAP (mmHg) 95.69±10.67 99.97±10.62 <0.001
Insulin (µU/mL)* 13.82±10.41 11.10±6.03 0.220
HOMA-IR* 82.54±105.73 57.14±30.12 0.240

Table 2. Framingham risk scores by age groups

<table>
<thead>
<tr>
<th>Age groups (years)</th>
<th>No. of individuals according to FRS category</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low risk</td>
</tr>
<tr>
<td>20-29</td>
<td>79 (100.0)</td>
</tr>
<tr>
<td>30-39</td>
<td>138 (98.6)</td>
</tr>
<tr>
<td>40-49</td>
<td>250 (91.9)</td>
</tr>
<tr>
<td>50-59</td>
<td>255 (73.5)</td>
</tr>
<tr>
<td>≥ 60</td>
<td>62 (36.7)</td>
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</tbody>
</table>

Percentages are in parenthesis
$\chi^2 (4) = 258.91; p <0.0001$

Table 3. Prevalence of metabolic syndrome and phenotypes by Framingham risk score

<table>
<thead>
<tr>
<th>Metabolic syndrome phenotypes</th>
<th>FRS category</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Low risk</td>
</tr>
<tr>
<td>High WC</td>
<td>228 (29.1)</td>
</tr>
<tr>
<td>High TG</td>
<td>341 (43.5)</td>
</tr>
<tr>
<td>High FBG</td>
<td>164 (20.9)</td>
</tr>
<tr>
<td>High BP</td>
<td>368 (46.9)</td>
</tr>
<tr>
<td>Low HDL</td>
<td>262 (33.4)</td>
</tr>
<tr>
<td>MS</td>
<td><strong>208 (26.5)</strong></td>
</tr>
</tbody>
</table>

High WC when WC > 90 cm in male and WC > 80 cm in female; high TG when TG ≥ 150 mg %; high FBG when FBG ≥ 100 mg %; high BP when SBP ≥ 130 mmHg or DBP ≥ 85 mmHg; low HDLc when HDLc < 40 mg % in male and HDLc < 50 mg % in female.

Figure 1. Prevalence of clustering of CVD risk factors in an individual by FRS category
DISCUSSION

Virtually no study on the efficacy of FRS was performed particularly among rural adult population in India. The present community based cross-sectional study was carried out to find out the efficacy of FRS in estimating CVD risk in a rural adult population in West Bengal, India.

In the present study, the higher anthropometric measures, body compositions, lipid profiles and blood pressure were found with increasing FRS category. In earlier studies, various cut-offs were used for the determination of adverse CVD risk factors. For example, MS were assessed by cut-offs such as World Health Organization (WHO), National Cholesterol Education Program Adult Treatment Panel (NCEP ATP III), International Diabetes Federation (IDF), South Asian Specific (SAS). To identify the population prevalent to diabetes but not diagnosed, cut-offs such as Indian diabetes risk score (IDRS) was used. The leisure time sedentary behaviour, marked as TV watching, was associated with adverse CVD risk factors. Earlier study further showed that the prevalence of adverse CVD risk factors was evident in according to age.

In the present study, though significant (p<0.0001) differences of FRS was found by age-group categories, individuals only in the age group of ≥ 60 years were found mostly in the ‘intermediate to high risk’ and were found more vulnerable. But as age is one of the components of FRS, it is not any surprising phenomena.

Though some of the MS phenotypes were rising but overall no remarkable change of MS was observed with increasing FRS category. Hence, it may be argued that FRS may not be considered as a good screening tool for the assessment of MS and its phenotype in this population.

Further, higher prevalence of some of the CVD risk factors clustering was found with increasing FRS, whereas, no remarkable higher prevalence of some of other CVD risk factors clustering was found with increasing FRS. It was already reported that cardiometabolic risk is high in the presence of one of the risk factors, presence of two doubles it and with three, the risk becomes eight fold. Therefore, it may be assumed that FRS may not be fit to categorize the study population distinctly in according to CVD risk factors clustering.

It was observed in earlier study that FRS was a good predictor of CVD risk factors. It is noteworthy to mention that CVD risk prediction cut-offs in limited resource settings have a very important role. The cut-offs should sufficiently distinguish between the high and low CVD risk so as to optimize treatment for those who will benefit the most. It was found that the majority of participants (~78%) were under ‘low risk’ and only ~22% participants were at ‘intermediate or high risk’ in the study population. This may have detrimental effect to the prevention and control of CVD since resources would be spent on screening, yet ‘high risk’ individuals would be under-identified, leading to higher rates of undertreatment and subsequently more complications. It may scatter any preventive effort.

Therefore, we may conclude that in the present study FRS could not discriminate the study population properly in respect of CVD risk. The better discriminatory performances of IDRS and FBG tertiles were found compared to FRS in the study population. However, similar modified scores may be developed for the study of CVD risk of this population more accurately considering ethnic and demographical variations of the study area. However, some limitations are associated with the present study. Though the sample size was sufficient enough, yet, it is not representative of the entire Indian adult population. Due to considerable ethnic and cultural heterogeneity in Indian population, further studies are required on other ethnic groups of urban as well as rural population of India to find out whether the same trend exists among them. Moreover, studies should be undertaken among the ‘Indian Diaspora’ worldwide to elucidate if they also show similar trends to that of sedentes in India or local population of the respective countries.

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REFERENCES


