



Low Framingham Risk Score Despite High Prevalence of Metabolic Syndrome in Asymptomatic North-Indian Population

M Bansal*, S Shrivastava**, R Mehrotra*, V Agarwal*, RR Kasliwal*

Abstract

Background : Conflicting data exists regarding relationship between the Framingham risk score (FRS) and presence of metabolic syndrome (MS). Strong influence of age on FRS may further modify this relationship as prevalence of MS at younger age increases in South-Asian countries including India. However, only limited information is available about the prevalence of MS and its relationship with FRS in such populations at present.

Methods : Clinical examination and biochemical investigations were performed in 1905 asymptomatic office executives who underwent routine health check-up at a tertiary care centre in India during the year 2005. Diagnosis of MS and FRS were based on the modified National Cholesterol Education Program- Adult Treatment Panel III guidelines.

Results : Mean age of the subjects was 45.2 ± 10.3 years and 71.8% were males. MS was present in 47.5% (905 of 1905) subjects. Overall, 76.8% patients with MS had 10-year cardiovascular (CV) risk <10%, 20.6% had 10-20% risk and only 2.7% had >20% risk according to FRS. In the lowest age-quartile, 95.9% patients had 10-year risk <10%, 4.1% patients had 10-20% risk and none had >20% risk. In contrast, in the highest age-quartile, less than half of the patients had 10-year risk <10% and nearly half had 10-20% risk of CV events.

Conclusions : Although the prevalence of MS is markedly high in young asymptomatic Indians, majority have low 10-year risk of CV events as estimated by FRS. These findings necessitate continued emphasis on detection of MS in these populations as reliance on FRS alone may result in underestimation of CV risk in them. ©

INTRODUCTION

Increasing prevalence and recognition of metabolic syndrome (MS) in recent years have spurred considerable interest in defining its role as a tool for cardiovascular (CV) risk prediction. However, despite a lot of research, it remains debatable whether MS has incremental value over Framingham risk scoring (FRS) as a marker of future CV risk. Several studies have demonstrated that presence of MS is associated with increased risk of adverse CV events beyond the risk imparted by the individual risk factors alone.¹⁻³ On the other hand, there is equally impressive data to suggest that CV risk is predicted better by FRS as compared to MS and that the entity 'MS' is no better than its individual components as a CV risk marker.⁴⁻⁶ Consequently, it has been argued that attempts to use the label 'MS' are likely to result in unwarranted investment of resources and may often be misleading to the clinicians as well as the patients.⁷

Notwithstanding these critiques, MS offers certain advantages over FRS. It is well established that FRS is heavily dependent on age and therefore underestimates risk of CVD in young individuals.^{8,9} In addition, FRS, being a marker of relatively short-term risk (10-year), may not be the optimal risk assessment strategy in young individuals who have life expectancy exceeding 25-30 years.¹⁰ In contrast, MS, owing to its excellent predictive accuracy for future development of diabetes mellitus (DM),¹ may be a better predictor of CV risk over long-term.¹¹ This issue is especially pertinent for the populations in which CV disease is becoming increasingly common at younger age such as the South Asians.¹² In these populations, not only the incidence of CVD is increasing at a younger age, MS is also becoming commoner¹³ and hence it is likely that a substantial proportion of the population would be having MS and yet be considered to have a low risk of CV events according to FRS. Unfortunately, very limited information is available regarding the Framingham risk status, prevalence of MS as well as the relationship between the two in such populations at present. The present study was therefore undertaken to determine the

*Indraprastha Apollo Hospital, New Delhi. **Escorts Heart Institute and Research Centre, New Delhi - 110 025, India.
Received : 6.8.2008; Revised : 20.10.2008; Accepted : 3.11.2008

prevalence of MS and its relationship with FRS in a North Indian population.

MATERIAL AND METHODS

One thousand nine hundred and five apparently asymptomatic office executives who underwent routine health check-up at a tertiary care centre in New Delhi during the year 2005 were included in the study. The individuals who had pre-existing cardiovascular disease (CVD) or had symptoms suggestive of CVD were excluded. All subjects underwent comprehensive clinical evaluation and biochemical investigations. The clinical assessment included detailed history regarding presence or absence of conventional CV risk factors (CVRFs), symptoms suggestive of any cardiovascular illness, general physical examination [including height, weight & blood pressure (BP) measurement] and the examination of cardiovascular system. Biochemical investigations included fasting and 2 hour post-prandial plasma glucose estimation and fasting lipid profile. The study was approved by the institutional review board.

Diagnosis of metabolic syndrome

MS was diagnosed using the recently updated Adult Treatment Panel (ATP III) criteria¹¹ that require presence of any three of the following five criteria to constitute a diagnosis of MS- a) BP >130 mm Hg systolic or > 85 mm Hg diastolic or already on antihypertensive drug treatment, b) serum triglycerides > 150 mg/dl or on drug treatment for elevated triglyceride levels, c) HDL-cholesterol <40 mg/dl in men and <50 mg/dl in women or on drug treatment for reduced HDL-cholesterol, d) fasting plasma glucose > 100 mg/dl or on drug treatment for elevated blood glucose and e) waist circumference greater than the cut-offs specified for the specific population. Since waist circumference was not available for all the patients in our study, we used body-mass index (BMI) > 25.0 kg/m² as a marker of obesity instead of waist circumference. The cut-off value of ≥ 25.0 kg/m² was used in accordance with the recommendations of the American Association of Clinical Endocrinologists for the diagnosis of MS.¹¹ Although most of the guidelines have recommended lower thresholds to define obesity in Asian populations¹⁴ and a much lower cut-off values for BMI have been proposed by various investigators,¹⁵ we have used a conservative definition similar to the one used in many previous studies.¹⁶

Framingham risk scoring

FRS was calculated using the standard algorithm.¹⁷ Based on FRS, individuals were categorized as being at low-risk (10-year risk- <10%), intermediate-risk (10-year risk- 10-20%) or high-risk (10-year risk- > 20%) of CV events. In addition, as per the recent American Heart Association (AHA) and ATP III recommendations to treat diabetes mellitus as 'coronary artery disease (CAD) risk equivalent',¹⁷ a separate Framingham risk scoring (FRS_{DM}) was also performed considering all patients with diabetes mellitus to have > 20 percent 10-year risk of CV events. Thus all the individuals

with diabetes mellitus were assigned to the high-risk category according to FRS_{DM}.

Statistical methods

The data was managed on Microsoft excel spreadsheet (version 2003, Microsoft Corp, Seattle, Washington). Values were expressed as mean (\pm standard deviation) or as percentages. Comparisons between the groups were done using Student's unpaired t test or Chi square test wherever appropriate. A p value <0.05 was considered statistically significant. All statistical analyses were done using SPSS for Windows (release 14.0, SPSS Inc).

RESULTS

Mean age of the patients was 45.2 ± 10.3 years and 71.8% (n=1368) were males. Metabolic Syndrome was present in 47.5% (905 of 1905) patients. The prevalence of MS was same in both men and women. Clinical and biochemical characteristics of the entire study population as well as the patients with or without MS are described in the Table 1. As expected, patients with metabolic syndrome had higher prevalence of hypertension and diabetes mellitus; had higher serum triglyceride levels and had lower HDL-cholesterol levels. In addition, family history of premature CAD was also commoner in patients with MS.

The prevalence of MS increased progressively with increasing age with 33.6% patients in the lowest age-quartile having MS as compared to 52.6% patients in the highest age-quartile (p value <0.001) (Fig. 1). Of the individual components of MS, increased blood pressure and obesity were the most prevalent and were seen in 90.6% and 81.1% of the MS patients respectively (Fig. 2). The prevalence of increased blood pressure, impaired fasting glucose and obesity increased with increasing age whereas low HDL-cholesterol was commoner at a younger age (Fig. 3).

Framingham risk score and metabolic syndrome

Overall, 76.8% patients with MS had 10-year CV risk <10%, 20.6% had 10-20% risk and only 2.7% had >20% risk according to FRS. Even with FRS_{DM}, nearly 60% patients belonged to low-risk category and only a quarter were deemed to be in the high risk category (Fig. 4).

Influence of age on the relationship between FRS and MS

The discrepancy between FRS and presence of metabolic syndrome was the most marked at the younger age and decreased with increasing age. In the lowest age-quartile, 95.9% patients had 10-year risk <10% according to FRS, 4.1% patients had 10-20% risk and none had >20% risk. In contrast, in the highest age-quartile, less than half of the patients had 10-year risk <10% and nearly half had 10-20% risk of CV events. Similar trends were seen with FRS_{DM} also. In the lowest age-quartile, 86.3% patients belonged to the low-risk category whereas only 29.1% patients belonged to the same category in the highest age-quartile (Fig. 5).

DISCUSSION

The present study has revealed that - 1) in a relatively

Table 1 : Clinical characteristics of the study population

Parameter	All patients	No MS	MS
Age (years)	45.2 ± 10.3	43.6 ± 10.9	46.9 ± 9.3*
Male sex	1368 (71.8%)	718 (71.8%)	650 (71.8%)
Body-mass index (kg.m ²)	25.7 ± 3.9	24.1 ± 3.4	27.4 ± 3.5*
Hypertension	876 (46.0%)	311 (31.1%)	565 (62.4%)*
Diabetes	268/1891 (14.2%)	38/992 (3.8%)	230/899 (25.4%)*
Family history of premature CAD	224 (11.8%)	101 (10.1%)	123 (13.6%)*
Current smoking	239 (12.5%)	125 (12.5%)	114 (12.6%)
Systolic blood pressure (mmHg)	131.1 ± 13.5	127.0 ± 12.7	135.6 ± 12.9*
Diastolic blood pressure (mmHg)	81.7 ± 8.7	80.1 ± 7.8	83.5 ± 9.3*
Fasting plasma glucose (mg/dl)	102.0 ± 31.6	93.0 ± 17.4	111.8 ± 39.8*
Total cholesterol (mg/dl)	192.0 ± 38.8	188.2 ± 37.6	196.2 ± 39.7*
Triglycerides (mg/dl)	150.8 ± 89.8	116.9 ± 62.1	188.3 ± 100.2*
HDL-cholesterol (mg/dl)	45.5 ± 10.6	49.2 ± 10.7	41.5 ± 8.8*
LDL-cholesterol (mg/dl)	119.4 ± 31.8	116.5 ± 31.4	122.7 ± 31.9*
Serum uric acid (mg/dl)	6.2 ± 1.5	5.9 ± 1.5	6.5 ± 1.5*

MS- metabolic syndrome; *- p value <0.05 for comparison between patients with and without metabolic syndrome

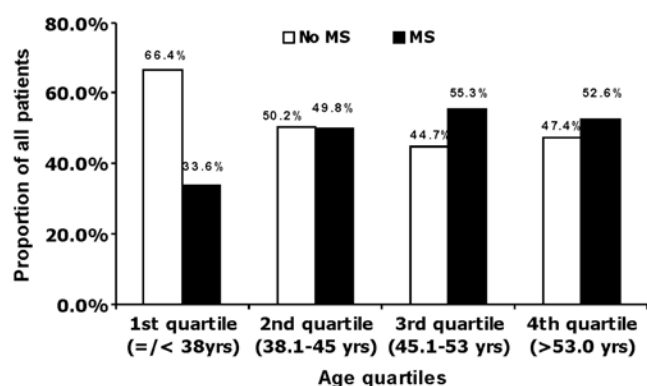


Fig. 1 : Prevalence of metabolic syndrome in different age quartiles of the entire study population.

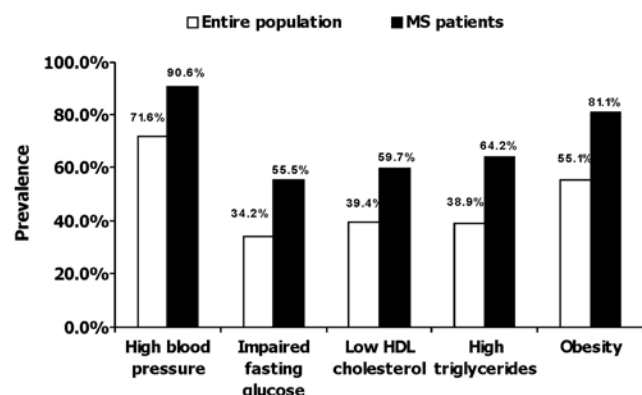


Fig. 2 : Prevalence of individual components of metabolic syndrome in the entire study population and in the patients with metabolic syndrome.

young asymptomatic North-Indian population, prevalence of MS is markedly high, 2) majority of the patients with MS have low 10-year risk of CV events as estimated by FRS and 3) the discrepancy between MS and FRS is maximum at younger age and decreases as the age increases.

Prevalence of metabolic syndrome

Most of the studies conducted in the western populations

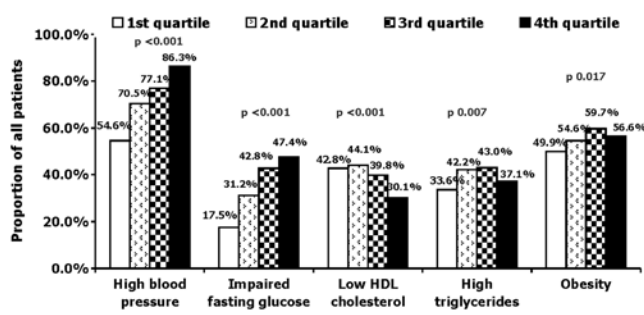


Fig. 3 : Influence of age on the prevalence of individual components of metabolic syndrome in the entire population.

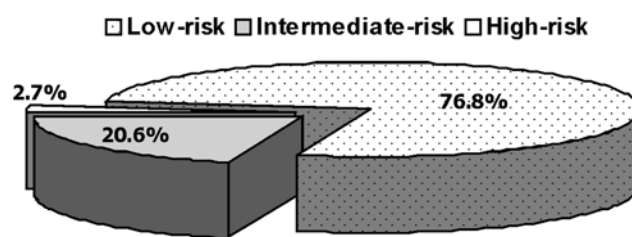


Fig. 4a

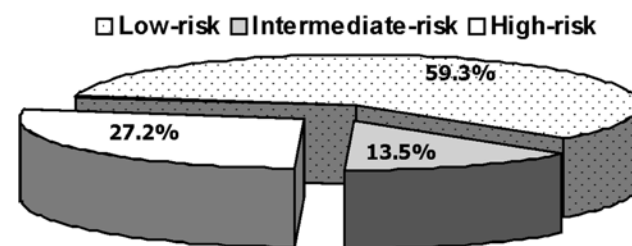


Fig. 4b

Fig. 4 : Prevalence of Framingham risk groups in the population with metabolic syndrome. 4a) Conventional Framingham risk scoring, 4b) diabetics included in the high-risk group.

have reported MS to be present in one-quarter to one-third individuals.^{3-5,18,19} The prevalence of MS in U.S. population was 23.1% in National Health and Nutrition Examination Survey (NHANES) - III and 26.7% in NHANES 1999-2000.¹⁸ Even when the revised NCEP-ATP III criteria were applied, the prevalence was 28.0% and 31.9% respectively in the two surveys. In the NHANES 1999-2000, the prevalence

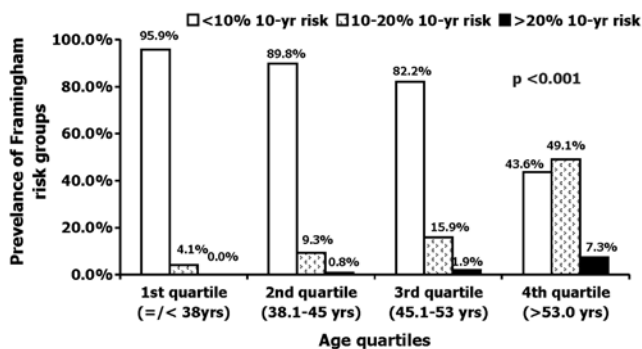


Fig. 5a

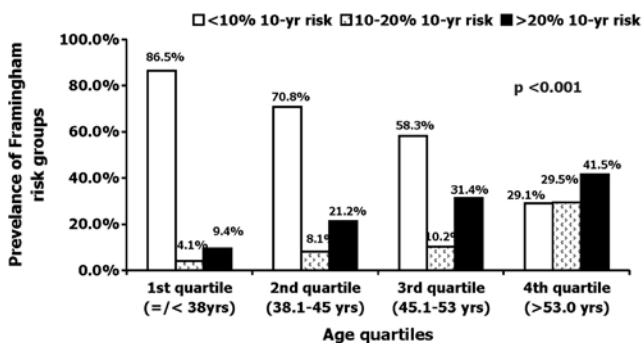


Fig. 5b

Fig. 5 : Influence of age on the prevalence of Framingham risk groups in the patients with metabolic syndrome. 5a) Conventional Framingham risk scoring, 5b) Diabetics included in the high-risk group

increased with increasing age from 16.5% among men aged 20 through 39 years to 40.3% in the age group 40 through 59 years to 46.4% among those older than 59 years.¹⁹ In the Framingham offspring study that included subjects between ages 50-81 years, 30.3% men and 24.7% women were found to have MS.³ A higher prevalence has been reported in few other studies. In a subgroup of the British regional heart study, 26% non-diabetic subjects (age 40-59 years) had MS⁴ whereas in a sample from San Antonio heart study (age 25-64 yrs), MS was present in 32.2% subjects.⁵

Studies conducted in resident Indians have reported variable figures for the prevalence of MS. In a recent epidemiological study, Deepa M et al reported 25.8% prevalence of MS according to the International Diabetes Federation criteria and 18.3% according to the original ATP III criteria (which utilized much higher cut-off values for waist circumference as currently accepted).²⁰ In contrast, in a study on 475 subjects aged 20-75 years, Ramachandran et al found MS to be present in 41.1% patients and the prevalence was even higher (>70%) in patients with elevated fasting glucose levels.¹³ Similarly, in a community survey involving 226 men and 232 women, Gupta et al reported the prevalence of MS to be 36.2% in men and 47.8% in women.²¹ Our finding of high prevalence of MS is thus more consistent with these data and may reflect inclusion of select population of office-executives. These subjects, owing to the nature of their job, are more likely to have a sedentary life-style and may also be exposed to faulty dietary habits, thereby increasing the risk of developing MS. In addition, as discussed in the

limitations, it is possible that our study, being a hospital-based study, might have overestimated the prevalence of MS to some extent. Nonetheless, our findings suggest significantly high prevalence of MS in office executives in North India.

In our study, we found prevalence of MS was similar in men and women. This is in contrast to many of the previous studies that have reported higher prevalence of MS in women as compared to men.^{20,21} This discrepancy may be explained by the use of BMI (which has same cut-offs for men and women) instead of waist-circumference (has lower cut-offs for women) as the criterion for obesity in the present study.

Framingham risk score and metabolic syndrome

FRS has traditionally been the standard CV risk assessment tool worldwide and many of the current guidelines regarding use of statins, aspirin etc for primary prevention of CV disease require estimation of FRS for decision making.¹⁷ However, it is noteworthy that the Framingham risk equations are derived from a western population and may not be applicable to South Asians who are believed to be genetically different and tend to have high prevalence of most of CV risk factors at a younger age.^{12,22} A recent study has explicitly demonstrated increased risk of developing CAD at a younger age in diabetic Indians.²³ In this study involving 1087 diabetics, the authors found that transition from low to moderate-risk category occurred at age 37 years for men and at 50 years for women, much lower than the same for western populations. Thus, it is likely that FRS may not be the best CV risk-assessment tool for Indian subjects and role of other risk markers, including MS, for this purpose needs to be evaluated.

Numerous studies have been conducted in past to evaluate the relative merits of MS and FRS for prediction of CV risk but have shown inconsistent results.¹⁻⁶ However most of these studies have been conducted in the older populations and/or have had a follow-up of only 5 to 10 years.^{1,3,5} As already mentioned, FRS being heavily dependent on age, underestimates CV risk in young individuals.^{8,9} Furthermore, FRS does not include several prominent features of MS such as obesity, hypertriglyceridaemia and elevated high sensitivity-C reactive protein levels which are considered to be independent risk factors for cardiovascular disease (CVD).¹⁷ Some of these risk factors esp. fasting hyperglycemia (not amounting to diabetes), obesity etc. are known to impart CV risk over long-term rather than a relatively shorter 5-10 year period.¹¹ Hence, the addition of these risk factors to FRS in previous studies has not been shown to make any appreciable impact on its ability to predict 10-year risk of CV events.⁶ Thus, it still remains to be determined whether FRS or MS is a better risk assessment tool in young individuals. In a recent study, Zarich et al evaluated 165 consecutive subjects of age <45 years who presented with acute myocardial infarction.²⁴ MS was found to be present in almost two thirds of these subjects. Excluding subjects with diabetes (23% of the entire

cohort), the mean 10-year FRS in the total cohort was 9.3%, with 62% patients belonging to the lowest risk category and only 17.1% subjects having a 10-year risk greater than 20%. Among the patients with MS, only 28% had a FRS greater than 20%. This study strongly suggests that the CV risk in young patients is probably underestimated by FRS. In the present study involving over nineteen hundred asymptomatic subjects, we have also demonstrated that MS is highly prevalent even at a young age and the majority of these patients have low 10-year CV risk as estimated by the FRS. Similar results were obtained in an analysis of 3323 Framingham offspring men and women (mean age- 52 years). Ten-year risk in men with MS generally ranged from 10% to 20% whereas in women the 10-year risk for CHD did not exceed 10%. In the entire cohort, MS alone predicted ~25% of all new-onset CVD over an 8-year follow-up.⁶ Our findings thus reinforce these data.

Furthermore, in the present study, we found that family history of premature CAD was also commoner in patients with MS. Whether this finding reflects deleterious influence of faulty life-style patterns in these families or of genetic make-up or a combination of both was not apparent from the present study. Nonetheless, as family history of premature CAD is also a recognized major risk factor for CAD¹⁷ and is not included in FRS, it further lends support to our hypothesis that FRS may not be the optimal risk assessment tool in these patients.

Although we were unable to demonstrate whether MS is a better predictor of CV risk than FRS in the studied population owing to the cross-sectional nature and the lack of patients with established CVD in our study, our findings have significant implications for risk assessment in Indian subjects. The incidence of CVD in young individuals is increasing rapidly in India and other South Asian nations and there is an urgent need to implement aggressive preventive strategies to curb the 'CVD epidemic' in this region. A low FRS in these population groups, which are otherwise at high risk of developing CVD, will not only be misleading, but may also lead to a sense of complacency and a lack of intensification of preventive strategies. In contrast, recognition of MS in these subjects may help in more aggressive implementation of the non-pharmacological as well as pharmacological strategies to prevent development of CVD. Nevertheless, it must also be remembered that mere presence of MS does not necessarily imply increased future risk of CV events. Although it is still debatable, previous studies have argued that MS does not have incremental prognostic value over its individual components.⁴⁻⁶ However, as already mentioned, most of these studies have evaluated prognostic value of MS over 5-10 years period which is not a desirable end-point in younger subjects. A diagnosis of MS in young subjects will at least alert the treating physician as well as the patient himself, of the possible risk of developing diabetes and CV disease over long-term. However, it needs to be proven whether such an approach would actually lead to reduction in CVD incidence and prevalence in a cost- and effort-effective manner.

LIMITATIONS

As already discussed, the two major limitations of our study were its cross-sectional nature and the lack of patients with established CVD which did not allow us to evaluate whether MS is a better marker of CV risk than FRS in these individuals. Nevertheless, the study conveys an important message that reliance on FRS alone may jeopardize efforts to prevent CVD in the subjects in whom the prevalence of CVRFs is high at a younger age. Our data is significant since it has been derived from a large population cohort. In addition, since we did not selectively recruit young subjects (unlike many previous studies), our findings more accurately reflect the current CV risk status of these populations. To the best of our knowledge, ours is the only study other than the above mentioned Framingham data (detailed results have not been published yet) that has demonstrated such findings.

Another limitation of our study was the lack of waist circumference measurements for the study subjects. Although waist circumference is generally preferred over BMI as a marker of obesity for the purpose of CV risk assessment, we believe that use of BMI instead of waist-circumference in the definition of MS did not substantially alter our findings. BMI has been shown to correlate very well with waist circumference in several studies. In the NHANES III, measurements obtained from ~15000 participants indicated that the correlation coefficient between BMI and WC was > 0.9 irrespective of the age, sex, or ethnicity of groups evaluated.²⁵ In another study, no difference was found in the correlation between degree of adiposity and insulin resistance irrespective of the parameter (BMI or WC) used as the index of obesity.²⁶ Moreover, the definitions of MS recommended by the WHO and the American Association of Clinical Endocrinologists have also used BMI as an index of obesity.⁶

Finally, our study was a hospital-based study and possibility that this may have introduced some referral bias can not be denied. However, it may be noted that the individuals who were enrolled in the present study were those who had undergone health check-up as part of preventive health program of their respective organizations and not because of the fact that they were already having one or more risk factors for CVD. Moreover, the primary purpose of the present study was to determine relationship between FRS and MS which was unlikely to be affected by possible over-inclusion of patients with MS.

CONCLUSIONS

In conclusion, the present study demonstrates high prevalence of MS at a younger age in asymptomatic North-Indian office-executives. Since the majority of these subjects had low CV risk according to FRS despite high prevalence of MS, it is possible that the sole reliance on FRS may result in inappropriate underestimation of long-term CV risk in these subjects. Prospective studies are needed to determine optimal CV risk assessment strategy in such populations.

Until such studies are performed, it is advisable to continue emphasizing on recognition and management of MS in these populations.

Acknowledgements

The study was supported by a research grant from the Pfizer Limited, India. We are also extremely thankful to Mr Y S Shulimkiu Tikhir for his assistance with the data collection.

REFERENCES

1. Sattar N, Gaw A, Scherbakova O, et al. Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Prevention Study. *Circulation* 2003;108:414-9.
2. Gami AS, Witt BJ, Howard DE, et al. Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. *J Am Coll Cardiol* 2007;49:403-14.
3. Najarian RM, Sullivan LM, Kannel WB, Wilson PW, D'Agostino RB, Wolf PA. Metabolic syndrome compared with type 2 diabetes mellitus as a risk factor for stroke: the Framingham Offspring Study. *Arch Intern Med* 2006;166:106-11.
4. Wannamethee SG, Shaper AG, Lennon L, Morris RW. Metabolic syndrome vs Framingham Risk Score for prediction of coronary heart disease, stroke, and type 2 diabetes mellitus. *Arch Intern Med* 2005;165:2644-50.
5. Stern MP, Williams K, Gonzalez-Villalpando C, Hunt KJ, Haffner SM. Does the metabolic syndrome improve identification of individuals at risk of type 2 diabetes and/or cardiovascular disease? *Diabetes Care* 2004;27:2676-81.
6. Grundy SM, Brewer HB, Jr., Cleeman JI, Smith SC, Jr., Lenfant C, for the Conference P. Definition of Metabolic Syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association Conference on Scientific Issues Related to Definition. *Circulation* 2004;109:433-8.
7. Kahn R. Metabolic Syndrome: Is It a Syndrome? Does It Matter? *Circulation* 2007;115:1806-11.
8. Berry JD, Lloyd-Jones DM, Garside DB, Greenland P. Framingham risk score and prediction of coronary heart disease death in young men. *Am Heart J* 2007;154:80-6.
9. Hemann BA, Bimson WF, Taylor AJ. The Framingham Risk Score: an appraisal of its benefits and limitations. *Am Heart Hosp J* 2007;5:91-6.
10. Lloyd-Jones DM, Wilson PW, Larson MG, et al. Framingham risk score and prediction of lifetime risk for coronary heart disease. *Am J Cardiol* 2004;94:20-4.
11. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and Management of the Metabolic Syndrome: An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation* 2005;112:2735-2752.
12. Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular diseases: part I: general considerations, the epidemiologic transition, risk factors, and impact of urbanization. *Circulation* 2001;104:2746-53.
13. Ramachandran A, Snehalatha C, Satyavani K, Sivasankari S, Vijay V. Metabolic syndrome in urban Asian Indian adults—a population study using modified ATP III criteria. *Diabetes Res Clin Pract* 2003;60:199-204.
14. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* 2004;363:157-63.
15. Misra A, Wasir JS, Pandey RM. An Evaluation of Candidate Definitions of the Metabolic Syndrome in Adult Asian Indians. *Diabetes Care* 2005;28:398-403.
16. Ishizaka N, Ishizaka Y, Hashimoto H, Toda E-I, Nagai R, Yamakado M. Metabolic Syndrome May Not Associate With Carotid Plaque in Subjects With Optimal, Normal, or High-Normal Blood Pressure. *Hypertension* 2006;48:411-417.
17. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Final Report. *Circulation* 2002;106:3143-3421.
18. Ford ES, Giles WH, Mokdad AH. Increasing prevalence of the metabolic syndrome among U.S. adults. *Diabetes Care* 2004;27:2444-9.
19. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. *JAMA* 2002;287:356-9.
20. Deepa M, Farooq S, Datta M, Deepa R, Mohan V. Prevalence of metabolic syndrome using WHO, ATPIII and IDF definitions in Asian Indians: the Chennai Urban Rural Epidemiology Study (CURES-34). *Diabetes Metab Res Rev* 2007;23:127-34.
21. Gupta R, Sarna M, Thanvi J, Rastogi P, Kaul V, Gupta VP. High prevalence of multiple coronary risk factors in Punjabi Bhatia community: Jaipur Heart Watch-3. *Indian Heart J* 2004;56:646-52.
22. Joshi P, Islam S, Pais P, et al. Risk factors for early myocardial infarction in South Asians compared with individuals in other countries. *JAMA* 2007;297:286-94.
23. Idris I, Deepa R, Fernando DJ, Mohan V. Relation between age and coronary heart disease (CHD) risk in Asian Indian patients with diabetes: A cross-sectional and prospective cohort study. *Diabetes Res Clin Pract* 2008;81:243-9.
24. Zarich S, Luciano C, Hulford J, Abdullah A. Prevalence of metabolic syndrome in young patients with acute MI: does the Framingham Risk Score underestimate cardiovascular risk in this population? *Diab Vasc Dis Res* 2006;3:103-7.
25. Ford ES, Mokdad AH, Giles WH. Trends in waist circumference among U.S. adults. *Obes Res* 2003;11:1223-31.
26. Farin HM, Abbasi F, Reaven GM. Body mass index and waist circumference correlate to the same degree with insulin-mediated glucose uptake. *Metabolism* 2005;54:1323-8.