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Assessing Cardiovascular Risk in Type 2 Diabetes Mellitus Patients Using United Kingdom Prospective Diabetes Study and Framingham Risk Score

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ABSTRACT

Background: Biomarkers have been suggested for cardiovascular risk estimation among patients with diabetes mellitus. The present study aims to assess the risk of developing cardiovascular disease among type 2 diabetes mellitus patients and to compare U.K. Prospective Diabetes Study (UKPDS) and Framingham Risk score. **Methods:** Known cases of type 2 diabetes mellitus from the outpatient clinic of our hospital were enrolled in the study. Demographic, clinical and laboratory investigation findings were noted and analysed. **Results:** The average risk for developing coronary heart disease in the next 10 years was 13.12% using UKPDS and 13.45% using the Framingham risk score. We observed that 8.3% and 1.6% of the patients had a high risk of developing CHD and fatal CHD respectively, while high risk of developing stroke and fatal stroke was in 1.6% and 0% of the patients respectively. Intermediate risk for developing CHD and fatal CHD was in 16.6% and 11.6% of the patients, while risk for developing stroke and fatal stroke was in 1.6% and 0% of the patients respectively. Among male patients, we observed that UKPD 56 score was higher than Framingham Risk score, though the difference was not statistically significant (18.2 vs 13.3; p value = 0.99). However, among female patients, UKPD 56 score was lower than Framingham Risk score, which was also statistically not significant (7.45 vs 13.6; p value = 1.00). **Conclusion:** Large sample multi-centric studies are required to assess the applicability of UKPDS and Framingham risk score in Indian population and help design a new assessment tool.

Keywords: Coronary heart disease; Diabetes mellitus; Risk assessment; UKPDS.

INTRODUCTION

The global burden of Type 2 diabetes mellitus is increasing in pandemic proportions, particularly in developing nations like India. Over the years, numerous studies have demonstrated that diabetes mellitus is associated with an increased all-cause cardiovascular morbidity and mortality. Diabetes poses two to four times higher risk for developing CVD as compared to general population. However, the increased cardiovascular risk associated with diabetes mellitus is determined by various factors and difficult to predict. Novel biomarkers have been suggested in the past which can help improve risk estimation among diabetics. The most widely used algorithm for people with diabetes mellitus is the U.K. Prospective Diabetes Study (UKPDS) risk score. This algorithm was developed based on large randomized controlled trial which showed that both intensive treatment of blood glucose and of blood pressure in diabetes can lower the risk of diabetes-related complications in individuals newly diagnosed with T2DM. In addition, the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and the Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) guidelines recommend using the Framingham risk scores to assess the absolute risk of type II diabetics developing CVD. The present study aims to assess the risk of developing cardiovascular disease among type 2 diabetes mellitus patients presenting to our hospital and to compare UKPDS and Framingham Risk score.

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MATERIALS AND METHODS

Study Design and Sampling

The present study was conducted in the Department of Medicine, Lokmanya Tilak Municipal General

Hospital and Medical College, Mumbai. We recruited patients, aged 25 to 65 years, who were known case of type 2 diabetes mellitus from the outpatient clinic of our hospital. Patients with a diagnosed coronary heart disease or stroke, outside the age group and those who had diabetes for more than 20 years were excluded from the study. The study was approved by the Institutional Ethics Committee. Eligible patients were approached by the investigators and were explained the purpose of the study. Those who agreed to participate were asked to sign a consent form before being enrolled in the study.

Biochemical analyses

A blood sample of all patients was collected following the interview in fasting state for assessing various lipid profile parameters and glycated haemoglobin. Level of HbA1c was determined using immunoturbidimetric method in a sample of a whole blood in K2EDTA. Other biochemical parameters were performed on the same analyzer, using spectrophotometric assay.

Data Collection and Data Analysis

Enrolled patients were followed up in special morning outpatient clinic, where they were asked to come in fasting state. Using a pre-designed semi-structured study proforma, the demographic and clinical information of the patients was noted. A physician took a medical history and performed a physical examination. The patient was considered a smoker if they smoked in the past month. Blood pressure was measured twice in the semi-recumbent position in the non-dominant arm with a mercury sphygmomanometer, and the average reading noted. Patients' 10-year risk for developing cardiovascular disease was calculated using UKPDS 56 for coronary heart disease and UKPDS 60 for stroke. UKPDS risk engine was calculated. Variables that were entered in the UKPDS risk engine equation were: age, sex, ethnicity, smoking status, atrial fibrillation status, diabetes duration, HbA1c, systolic blood pressure, total cholesterol, and high density lipid cholesterol. All participants were divided into three groups: low risk (< 15%), medium risk (≥15% and <30%), and high risk category (≥ 30%). Risk for developing coronary heart disease was calculated from Framingham Heart Study using age, smoking status, blood pressure, total cholesterol and HDL.

Data analysis was done by descriptive and analytic statistics using SPSS version 21.0 (SPSS Inc., New York, USA). Quantitative data were presented as means and standard error while qualitative data were presented as frequency distribution. We compared the means of UKPDS and Framingham Risk scores separately for males and females using the Student's t test. A p value less than 0.05 was considered statistically significant and 95% confidence intervals calculated.

RESULTS

Table 1: Baseline characteristics of the patients included in the study (all values are means)

Variables	Males (n=30)	Females (n=30)
Age (in years)	53.9	53.5
Age at diagnosis	47.6	48.6
Total cholesterol (mg/dl)	166.23	191.53
High density lipids (mg/dl)	39.06	48.23
Very low density lipids (mg/dl)	30.2	30.81
Glycated haemoglobin	8.34	8.5
Systolic blood pressure	117.8	123.9
Diastolic blood pressure	77.67	79.3

Table 2: Risk of developing coronary heart disease (CHD) or stroke among patients in the present study

Risk	Risk of developing CHD (Framingham Risk score)	Risk of developing fatal CHD (Framingham Risk score)	Risk of developing stroke (UKPDS 60)	Risk of developing fatal stroke (UKPDS 60)
High	05 (8.33%)	01 (1.66%)	01 (1.66%)	00 (00)
Intermediate	10 (16.66%)	07 (11.66%)	01 (1.66%)	00 (00)
Low	45 (75%)	52 (86.7%)	58 (96.7%)	60 (100%)

Table 3: Comparing risk assessments by UKPDS and Framingham Heart study among males and females

Gender	UKPDS 56 (mean and standard error)	Framingham Risk Score (mean and standard error)	Average difference between the two scores	P value
Males	18.2 (2.09)	13.3 (1.32)	5.5	0.99
Females	7.45 (0.65)	13.6 (1.11)	-6.15	1.00

In the present study, we included a total of 60 patients, with equal number of male and female patients. [Table 1] describes the baseline characteristics of the patients included in the study. Most common age group in both males and females was 40 to 60 years. Mean age at diagnosis of diabetes mellitus was 47.6 years for males and 48.6 for females. So the average number of years since diagnosis in females was 4.68 years and 6.64 years in males. While mean total cholesterol and high density lipids were found to be higher among female patients as compared to male patients, very low density lipids were similar among the two patient groups. Systolic and diastolic blood pressures were similar between males and females. [Table 2] describes the risk of developing CHD and stroke. The average risk for developing coronary heart disease in the next 10 years was 13.12% using UKPDS and 13.45% using the Framingham risk

score. We observed that 8.3% and 1.6% of the patients had a high risk of developing CHD and fatal CHD respectively, while high risk of developing stroke and fatal stroke was in 1.6% and 0% of the patients respectively. Intermediate risk for developing CHD and fatal CHD was in 16.6% and 11.6% of the patients, while risk for developing stroke and fatal stroke was in 1.6% and 0% of the patients respectively. Low risk of developing CHD and fatal CHD was in 75% and 86.7% of the patients, while risk for developing stroke and fatal stroke was in 96.7% and 100% of the patients. Among male patients, we observed that UKPD 56 score was higher than Framingham Risk score, though the difference was not statistically significant (18.2 vs 13.3; p value = 0.99). However, among female patients, UKPD 56 score was lower than Framingham Risk score, which was also statistically not significant (7.45 vs 13.6; p value = 1.00).

DISCUSSION

In the present study, the overall average risk for developing coronary heart disease in the next 10 years was 13.12% using UKPDS and 13.45% using the Framingham risk score. In a cross-sectional study of 199 asymptomatic T2DM patients, Rakhit et al reported that area under the curves (AUCs) of the FRS and UKPDS risk engine were 0.61 and 0.56, respectively, with no significant difference between them. Guzder et al compared the predictability of the FRS and UKPDS equations in 428 newly diagnosed T2DM patients in United Kingdom and reported that the AUCs of FRS and UKPDS were 0.657 and 0.670, respectively. Simmons et al estimated 10-year CVD risk in the DM group as 37% and 33% using the FRS and UKPDS equations respectively.[2] These evidence suggest that UKPDS and Framingham risk score can have variability in predicting risk. The UKPDS risk engine was developed for a large cohort of almost 5100 specifically newly diagnosed patients with DM2, during a median follow-up of 10.7 years, whereas Framingham Risk Score included almost 5580 individuals, but only 6% of them were known to have type 2 diabetes mellitus. Therefore, it is speculated that FRS tended to underestimate risk for people with type 2 diabetes mellitus.

It is also important to recognise that the choice of validation population will have an influence on the performance of a risk score in estimating CVD risk. The difference in the ethnicity of the population might affect the predictability of these two risk scoring systems. A systematic review of 27 external validity studies found that the performance of the FRS differs significantly among different countries and ethnic groups. Predicted to observed ratios using FRS ranged from an under prediction of 0.43 in a high risk population, to over-prediction of 2.87 in low risk populations. A weak concordance between predicted and actual cardiovascular risk was also reported by a systematic review. All these discrepant results may partly be explained by the fact that some ethnic groups have higher CVD risk than the others. For example, the UKPDS risk engine had moderate discrimination and poor calibration when evaluated in a Chinese diabetic population. This underlines the fact that the accuracy of a risk score largely relies on the background risk of a specific population to which it is applied. It may be more useful to develop or recalibrate population-specific risk prediction tools, rather than trying to find a universal risk score that will work in all populations.

In our study, UKPDS found higher risk among male patients and Framingham risk score found higher risk among female patients. This discrepancy might have been because of the difference in the duration of diabetes between males and females. As UKPDS factors in the duration of diabetes, higher risk was observed among males, who had a higher average duration of diabetes than females in our study. However, Framingham risk scores does not take in to account the duration of diabetes. Higher risk among males in our study was supported by the findings of Bansal et al, who studied 489 patients with newly diagnosed diabetes and found that high risk category on UKPDS was observed in 34% males and 12% females, while high risk category using Framingham risk score was observed in 26% males and 18% females.[10]

There are a few limitations of this study. First, our sample was enrolled from a tertiary care hospital, potentially being treated for various cardiovascular risk factors, which might inherently put them at a lower risk for developing cardiovascular complications. This may introduce selection bias. Second, ours being a cross-sectional study, patients were not followed over time to assess their final clinical outcomes. Last, ours is a small single centre sample. As a result we cannot comment on the overall applicability of UKPDS and Framingham risk score in the Indian population.

CONCLUSION

The present study estimates that the overall average risk for developing coronary heart disease in the next 10 years was 13.12% using UKPDS and 13.45% using the Framingham risk score. Keeping in view the high interethnic variability of UKPDS and Framingham risk scoring systems, large sample multi-centric studies are required to assess their applicability in Indian population and help design a new assessment tool.

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