ISCHAEMIC HEART DISEASE AND GLYCAEMIC CONTROL IN TYPE-2 DIABETES MELLITUS BY QUESTIONNAIRE METHOD

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Background: Various tests like Echocardiogram, Nuclear scan, Electron-beam computed tomography, Coronary angiography, and magnetic resonance angiography are available for diagnosis of ischemic heart disease (IHD). But most of these are expensive, invasive and cannot be afforded in developing countries. An attempt was made to study sensitivity, specificity, and predictive value of non-invasive technique like questionnaire method and compared with traditional clinical evaluation. This study compared diagnosis of angina made with the Rose Questionnaire to diagnosis by physician in type-2 diabetes mellitus and the effect of glycaemic control. Methods: A cross-sectional study was done from March 2005 to March 2006. Cases were collected from outpatients and inpatients visiting RL Jalappa hospital and SNR Hospital attached to Sri Devraj Urs Medical College Kolar, Karnataka, India. Glycosylated haemoglobin levels were estimated. Data on Rose questionnaire angina and physician diagnosed angina were collected and compared between groups of well controlled diabetics, poorly controlled diabetics and controls. The 12 lead Electrocardiogram was used to confirm the diagnosis. Results: The Rose questionnaire had 63.63% sensitivity, 97.5% specificity, 73% positive predictive value, and 96% negative predictive value. This study also showed the occurrence of IHD was higher in the poorly controlled diabetics (16.3%) as compared to well controlled diabetic patients (6%) and controls (5%) which were significant. Conclusions: The questionnaire diagnosis showed good sensitivity and high specificity as compared with diagnosis by physicians. The questionnaire method can be frequently used and incorporated in cardiovascular risk assessment and epidemiologic screening programs.

Keywords: Ischemic heart disease, glycosylated haemoglobin, type-2 diabetes mellitus, Rose angina questionnaire

INTRODUCTION

The Rose Questionnaire (RQ), also called as the London School of Hygiene Cardiovascular Questionnaire, has been frequently used in epidemiologic research as a standard, unbiased and validated measure of the prevalence of angina in general population surveys since its introduction in 1962. The RQ has been widely used in its original, modified forms, and in translation to study the prevalence and natural history of ischemic heart disease, response to interventions, and to make population comparisons. There is no agreed ‘gold standard’ which can be used to validate RQ measures of angina but studies have used expert clinical diagnosis, Electrocardiogram Findings, Exercise Thallium scans and coronary angiography. Clearly without such a standard the terms ‘sensitivity’ and ‘specificity’ need to be used with caution. The Questionnaire was found to have 81% sensitivity and 97% specificity when compared to clinical judgment.1-3

Diabetes mellitus (DM) is the commonest metabolic endocrine disease affecting mankind. The incidence of disease is on a rise not only in developed countries but also in developing countries. It is characterised by elevated fasting and postprandial blood glucose level and variety of multisystem complications, mainly in the blood vessels of eye, kidney, nervous system and integument. The complications are more prevalent among the people of lower socioeconomic status because of negligence, illiteracy, poverty etc. Ischemic heart disease, especially Myocardial Infarction (MI) has reached enormous proportions striking more and more young subjects especially in patients with diabetes mellitus. It will result in greatest health hazard which mankind has ever faced in coming years unless we are able to reverse the trends by concentrated results into its cause and its prevention.

This study was designed to test the sensitivity and specificity of questionnaire and to assess the relation between glycaemic control (assessed by glycosylated haemoglobin HbA1c) and the occurrence of IHD (as detected by Rose Angina Questionnaire) so that the risk factor can be identified earlier, prevented and treated.

MATERIAL AND METHODS

This study was a case- control study. The study group comprised of 1200 subjects above 30 years of age having Type-2 diabetes mellitus. The control group comprised of 400 subjects above 30 years of age. Cases were collected from outpatients and inpatients visiting RL Jalappa Hospital and SNR Hospital attached to Sri Devraj Urs Medical College Kolar, Karnataka, India.

Subjects with history of hypertension, lung or other cardiac disease, smoking and alcoholism, on any drug affecting lipid levels of plasma were excluded from the study. All subjects were interviewed by means of a
structured questionnaire for general demographic details, lifestyle, cardiovascular risk factors, history of myocardial infarction, and symptoms of angina according to the Rose angina questionnaire after the clearance from ethical committee. The physicians’ interviews occupied 15–30 minutes each, as compared with about 3–5 minute for the questionnaire. Those who fulfilled all the Rose criteria were classified as having Rose questionnaire angina (RQA). History was taken in detail and general physical examination was done.

Angina was defined as having pain or discomfort in the chest when walking uphill or hurrying and fulfilling all of the following criteria: (1) situated in the sternum or the left anterior chest with or without left arm; (2) caused the subject to stop or slow down; (3) went away when the subject stopped or slowed down; and (4) was relieved within 10 minutes by rest. Possible MI was defined as having experienced severe pain across the front of the chest, lasting for half an hour or more.

Blood Samples was collected between 7 AM to 8 AM after overnight fasting. Glycosylated haemoglobin was estimated by standard laboratory method as an index of long-term glycaemic control (up to 3 months). Resting 12-lead ECG was recorded finally to compare the diagnosis between questionnaire method and clinical method. A 12-lead ECG is used as the gold standard for confirming the IHD. Possible IHD was defined as large Q and QS waves and possible IHD with small Q and QS, ST depression, flattened or inverted T waves or complete left bundle branch block. Those who fulfilled all these criteria were classified as having physician diagnosed angina (PDA).

One thousand six hundred (1,600) male subjects were selected. They were grouped as study group including poorly controlled diabetics (Group A: HbA1c levels >8.0%) and well controlled diabetics (Group B: HbA1c levels <8.0%) based on their HbA1c levels and controls (Group C). Rose Angina questionnaire was used as a tool to detect Ischemic Heart Disease. Analysis of data thus collected was performed using SPSS version 8.0 for Windows. Continuous variables are expressed as the Mean±SD and qualitative data as percentages. Chi-square test of association was carried out to evaluate the association of IHD in different groups. The mean difference was taken as significant at \( p < 0.05 \). Conclusion was drawn based on outcome of this statistical treatment.

RESULTS

Table-1 shows the distribution of the subjects according to the age. The youngest subject in the study group is aged 32 years and the oldest aged 68 years. The frequency of IHD was 1.25% in 31–40 year age group. This increased with age, and was 2.41% among those aged 41–50 and 3.25% in those aged 51–60 years and above 4.25% above the age of 60 years.

Table-2 shows distribution of IHD in non diabetics. The youngest subject in the control group is aged 31 years and the oldest aged 69 years. The prevalence of IHD was 0.5% in 31–40 year age group. This increased with age, and was 0.75% among those aged 41–50 and 1.75% in those aged 51–60 years and above 2.0% above the age of 60 years.

Table-3 shows IHD is higher in the poorly controlled diabetics when compared to well-controlled diabetics and normal healthy controls. It also shows the association of glycaemia with macro vascular circulation (i.e., coronary artery disease).

Among 1,600 subjects, 154 (prevalence 9.6%) had angina pain on exertion and rest and 1446 (90.4%) had no chest pain. Among 1,200 diabetics, 134 (11.2%) had a classic symptom of ischemia. Whereas out of 400 controls, only 20 (5%) had ischemic symptoms. The relative risk (RR) among diabetics was 2.23 (95% confidence interval 1.6–2.8). The exposure rate of occurrence of ischemic heart disease in diabetes is 87% and in non diabetics was 73%. Statistical association between the diabetics and occurrence of IHD was highly significant \( (p<0.001) \).

Table-4 shows the sensitivity and specificity of Rose angina questionnaire. The number in table shows the actual positive and negative data confirmed by physician diagnosed angina (by clinical examination and ECG). The Rose diagnosis of angina had 63% sensitivity, 97% specificity, 92% positive predictive value, and 97% negative predictive value. The percentage of false positives is 2.48% and false negatives are 36%. The Rose Questionnaire has an acceptably high specificity and sensitivity.
DISCUSSION

Ischemic heart disease is still one of the leading causes of Myocardial infarction, with diabetes mellitus being the major risk factor with an increased risk of atherosclerosis either alone or in combination with other major risk factors such as diet, smoking, body weight etc. It has been found that patients with type-2 diabetes mellitus suffer from dyslipidaemia which in turn leads to various vascular complications. The prevalence of ischemic heart disease in diabetics in present study is 1.5–4.5% in comparison with similar studies and values. Ischemic heart disease was seen in poorly controlled diabetics (16.3%), well controlled diabetics (6%), and controls (5%). As compared to controls and well controlled diabetics, the occurrence of IHD is significantly higher in poorly controlled diabetics (Chi-square test 13.13, \( p \leq 0.001 \)). Increased levels of glycosylation may be a contributory factor to develop ischemic changes in diabetic patients.

Many others studied the sensitivity, specificity, and predictive value of non-invasive testing like questionnaire method and compared with traditional clinical evaluation and invasive technique of vascular disease in a defined population. The findings of the present study are in conformity with the earlier studies.

Rose questionnaire application to specific populations such as younger women, those after MI, self-administration, by mail has been examined. It has been used in the Health Surveys for England and the 1984–1986 Scottish Heart Health Study. Heyden \textit{et al.}, assessed variability in response to the questionnaire and suggests that this variation is a reflection of the natural history of the disease rather than unreliability of the questionnaire. The Rose questionnaire had sensitivity of 81% and a specificity of 97% when compared to clinical judgment.\(^3\)

Rose Questionnaire was compared with physician opinion in assessment of angina pectoris in the Beta-Blocker Heart Attack Trial in which post-myocardial infarction patients, half of whom were treated with propranolol and half with placebo. The physician diagnosis of angina identified more patients who suffered a subsequent fatal or nonfatal event than did the Questionnaire.\(^4\)

The prevalence and correlates of Rose Questionnaire angina were investigated in white women and men aged 30 years and above who participated in the Lipid Research Clinics Program. Among men, the prevalence of Rose angina increased with age from about 1% to 12%, while the prevalence among women ranged from about 3% to 6%\(^5\).

Age-adjusted prevalence rates of Rose angina were similar among black, white, and Mexican-American women.\(^6\) Another study compared the Questionnaire to exercise thallium test evidence of coronary artery disease. The Rose diagnosis of angina had 26% sensitivity, 79% specificity, 42% positive predictive value, and 65% negative predictive value.\(^6\) The finding of the present study is in conformity with the earlier studies.

Smith \textit{et al.} reported that prevalence of Rose angina was 7.0% in black women, 4.8% in white women, 5.0% in black men, and 5.7% in white men (\( p = 0.37 \)). Blacks were more likely to report angina if they felt they were not getting needed medical care.\(^9\)

Reeder \textit{et al.} showed socio-demographic variation in the prevalence of cardiovascular disease in Saskatchewan. The results from the Saskatchewan Heart Health Survey showed among men, the prevalence of definite angina increased gradually with age from 1.7% in the 18 to 34 year group, 3.8% in the 35–54 year group to 4.8% in the 55–74 year group, while the prevalence among women ranged from 2.5%, 4.0% to 7.1% in the same age groups.\(^10\)

Lampe \textit{et al.} studied chest pain by questionnaire and prediction of major ischemic heart disease events in men. In the whole cohort, the relative risks (95% CI) of a major ischemic heart disease event were 2.03 for angina only, 2.13 for possible myocardial infarction only and 4.50 for angina plus possible myocardial infarction, compared to no chest pain.\(^11\)

Women with Rose angina had a poorer cardiovascular risk profile.\(^12\) The Rose angina questionnaire has been extensively used in different cultural settings, but may not perform consistently in different ethnic groups. The prevalence of possible Rose angina and diagnosed angina in both South Asian and European men was 18% and 8%, respectively. Sensitivity for a doctor’s diagnosis was 21% in South Asian and 37% in European men.\(^13,14\) The findings of the present study are in conformity with these studies.

Bodgard, and Murphy \textit{et al.} in a multivariate analysis reported that men with Rose angina had an increased risk of cardiovascular death or hospitalisation 1.49 (1.33–1.66), myocardial infarction 1.63 (1.41–1.85) or heart failure 1.54 (1.13–2.10) compared with men without angina. Angina in middle age substantially increases the risk of death, myocardial infarction, heart failure and other cardiovascular events.\(^15,16\)

Formation of glycated haemoglobin is essentially reversible, and the blood levels depend on both the life span of the red blood cell (average 120 days) and the blood Glucose concentration. The glycated haemoglobin concentration represents the

| Table 4: Sensitivity and specificity of Rose Angina Questionnaire |
|-------------------|-------------------|-------------------|
|                   | Chest pain present | Chest pain absent |
| RQA               | IHD Present        | IHD Absent        | Total            |
| Positive          | 98                 | 36                | 134              |
| Negative          | 56                 | 1410              | 1466             |
|                   | 154                | 1446              | 1600             |

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\( ^9\) http://www.pps.org.pk/PJP/6-2/Yatish.pdf
integrated values for glucose over the preceding 6 to 8 weeks and offers a snapshot of the average blood sugar control for the past few months.17

Hassan et al, translated the Rose Questionnaire into a Bahasa Melayu version and used it cross-culturally, and to measure its inter-rater and intra-rater reliability.18 Ugurlu et al, showed prevalence of angina, MI and doctor-diagnosed IHD were not different between Behcet’s syndrome patients and non-Behcet’s syndrome controls in the whole study population and when males and females were separately analysed.19 S Graff-Iversen et al collected information by a short, three-item version of the Rose Angina Questionnaire.20 However probably not only glycaemic optimization but also lifestyle and diet intervention plays a role in the improvement of the different components of diabetes dyslipidaemia.

CONCLUSION

The questionnaire diagnosis showed reasonable sensitivity and high specificity as compared with diagnosis by physician. The questionnaire method can be frequently used in epidemiologic research as a standard, unbiased and validated measure of the prevalence of ischemic heart disease in general populations. The former can be usefully incorporated in cardiovascular risk assessment and screening programs.

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REFERENCES


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