Macrovascular Complications and their associated Factors among persons with Type 2 Diabetes in Karachi, Pakistan - a multi-center Study

A. K. Khuwaja,G. Rafique,F. White,S. I. Azam (Department of Community Health Sciences, The Aga Khan University, Karachi..)

Abstract

Objective: To assess the prevalence of macrovascular complications and factors associated with these complications among persons with Type 2 diabetes.
Methods: A multi-center, cross-sectional survey was conducted in three diabetes clinics of Karachi from November 2000 to April 2001. Six hundred and seventy-two persons were interviewed to determine the prevalence of ischemic heart disease (IHD), cerebrovascular disease (CVA) and diabetic foot (DF). Demographic data and co-variables obtained include age, sex, duration of diabetes, body mass index (BMI), smoking status, exercise habits and history of hypertension (HTN).
Results: Overall, 26.4%, 6.8% and 3.9% of individuals had IHD, CVA and DF respectively. Multiple logistic regression analysis showed that subjects having IHD were more likely to have HTN (AOR=1.88, 95% CI 1.31- 2.69), not performing regular exercise (AOR=2.09, 95% CI 1.39-3.17) and be current smokers (AOR=1.85, 95% CI 1.10-3.10). Subjects having CVA were more likely to have diabetes for more than 5 years (AOR=1.94, 95% CI 0.97-3.87). Males were more prone than females to have DF (AOR=3.48, 95% CI1.46-8.31). Those who had DF were more likely to have diabetes for more than 5 years (AOR=3.29, 95% CI 1.09-9.89) and of reporting current smoking (AOR=4.01, 95% CI1.49-10.71).
Conclusion: Large proportions of persons with Type 2 diabetes were suffering from preventable macrovascular complications in Karachi, Pakistan. There is a need to develop risk factor modification interventions to reduce the impact of long-term complications (JPMA 54:60;2004).

Introduction

Over 10% of people in the age group 25 years and above have Type 2 diabetes and an equal number are suffering from impaired glucose tolerance in Pakistan 1-3 such that incidence rates for diabetes will increase over the next decade. 4 It is estimated that by the year 2025, the lumber of persons with diabetes in Pakistan will rise to 14;5 million and will be ranked 4th, as compared to 4.3 million, ranked 8th, in the year 1995. 5 Diabetes Mellitus is a complex metabolic disease associated with a large variety of complications; it leads to greater than normal risk for all manifestations of atherosclerosis, including IHD, CVA, and peripheral vascular diseases (PVD). There is sufficient evidence to indicate that macrovascular complications are more common among persons with Type 2 diabetes than in those with Type 1 diabetes, 6 with an incidence twice that of microvascular complications. 7 It is also known that among persons with diabetes, mortality is incurred mainly due to complications related to atherosclerosis, which accounts for 0% of all deaths and 75% of hospitalizations for

diabetic omplications. 8 Furthermore, macrovascular complications re responsible for the major part of socioeconomic burden of the disease affecting the individuals, their families and le health care system of the country. It is estimated that for low-income Indian family having an adult with diabetes, 25% of income may be devoted to diabetes care. 9 In a s modeling lifetime costs of complications from Type diabetes, macrovascular disease was estimated to be largest cost component, accounting for 52% of management costs and 85% of cumulative costs complications over the first 5 years. 10 The development of macrovascular complication among persons with diabetes is known to be related certain factors such as increased age, 6,11 longer duration diabetes, 12 less physical activity, 13 history of smoking HTN, 8,14 and obesity. 15 There is considerable evidence suggest that modification of these factors results in' substantial decrease and delay in the development diabetes complications, disabilities and premature mortality. 13,16,17 So far not much work has been done in Pakistan this area. Given the alarming projected diabetes caseload the coming years and the associated high health care co of diabetes complications, there is an urgent need to identify, the burden of long term complications of diabetes, their associated factors and the disease pattern. This will have implications for planning prevention strategies, objectives of our study were to assess the prevalence" macrovascular complications and factors associated with these complications among persons with Type 2 diabetes: diabetes clinics in Karachi.

Research Design and Methods

This was a multi-center cross-sectional study conducted at three diabetes clinics in Karachi, the largest city of Pakistan, with a population of 10 millionl8 belonging to different socio-economic groups. Clinic A represented the private sector, clinic B was affiliated with a non- governmental organization (NGO) and clinic C was part of the public sector. All persons with Type 2 diabetes (previously referred to as non-insulin-dependent diabetes) attending these clinics for a follow-up visit during the study period (November 2000-April 2001) were included in the study. However, persons suffering from Type I diabetes (previously encompassed by the term insulin-dependent diabetes), Gestational diabetes (any degree of glucose intolerance with first recognition during pregnancy) or with macrovascular disease(s) prior to diagnosis of Type 2 diabetes, were excluded. The estimated sample size was 237 from each clinic (total 711) with 80% power and a equal to 0.05. The required sample size was achieved from clinics A and B; however, in clinic C we were able to enroll 190 subjects during the given study period. Nevertheless, the sample size was recalculated and found that it did not reduce the power of the study below 80% (as originally intended). A pre-tested structured questionnaire was used to collect information on socio-demographic and associated factors of macrovascular complications from study subjects. Exercise was defined as 'regular' if a person was doing at least 20 minutes exercise or at least 30 minutes brisk walk, four or more times per week. Respondents who were currently smoking and smoked at least 100 cigarettes in their lifetime were defined as 'current smokers'. Height and weight were obtained from patient's records and body mass index (BMI) was calculated as weight in kilograms divided by height in meter squared. Those who had BMI > 25 were labeled as 'high BMI'. Individuals were classified as hypertensive if they were previously diagnosed and currently on anti-hypertensive medication. IHD was considered to exist if there was a

history of angina or/and myocardial infarction elicited by the study subject and documented in medical records. CVA was labeled if there was history of stroke (cerebral infarction, hemorrhage or thrombosis), transient ischemic attack, hemiplegia or monoplegia or/and documented evidence. DF was defined as current or past history of foot ulcers, gangrene or amputation of any part of the extremities. Data was analyzed using Statistical Package for Social Sciences (SPSS). Frequencies for macrovascular complications were calculated for each of the patient groups attending the three diabetes clinics. Univariate analysis was done to assess the relationship between outcome variables and socio-demographic and associated factors for macrovascular complications of diabetes using the Chi- square test and crude odds ratios with 95% confidence intervals. Multivariate logistic regression was carried out to evaluate the combined effect of multiple factors associated with macrovascular complications among persons with Type 2 diabetes after adjusting for confounding variables. Results are represented in terms of odds ratios, which express the magnitude of the effect of each category on the outcome, relative to the reference category.

Results

The general characteristics of the study population are presented in table 1 . In clinic A, respondents had a slight predominance of males (54%), whereas in clinic 8 and clinic C the majority were females (69% and 61 % respectively). Sixty-five percent of subjects in all clinics were > 50 years of age and 59% found to have diabetes for more than 5 years. Generally, the individuals attending clinic A had a higher socio-economic status as compared to clinics 8 and C. Among the respondents with high 8MI, both males and females were equal in number in clinic A, while approximately three-quarters were females in clinics 8 and C (76% and 72% respectively). Only about 12% of individuals in the study were current smokers and majority (98%) were males. HTN was common among the study population varying from one third to half between different clinics, however, there was a female preponderance observed in all three clinics (A: 55%, B: 76% and C: 65%). The frequencies of macrovascular complications among males and females with Type 2 diabetes are given in figures I and 2. Overall, 26.4%, 6.8% and 3.9% of individuals had IHD, CVA and DF respectively. Males had more IHD in clinic A (34.6% vs 26.4%) arid clinic 8(29.3% vs 23.4%) while in clinic C females dominated (25.9% vs 18.9%). In both clinics A and B, the females had a higher proportion of CVA (5.5% and 3% respectively) while more males (8.1%) had CVA in clinic C. DF was predominantly found in males in all the 3 clinics. Results of univariate and multivariate analysis for factors associated with macrovascular complications among persons with Type 2 diabetes are summarized in table 2. In univariate analysis, the characteristics having statistically significant association between those who had IHD and those who did not were increased age, current smoking status, not practicing exercise regularly and positive history ofHTN. For CVA statistically significant associations were found with increased age and duration of diabetes of more than 5 years. For DF the characteristics demonstrating statistically significant associations were male sex, duration of diabetes for more than 5 years, current smoking status and not practicing exercise regularly. In the final multivariate model, positive history of HTN, not performing exercise regularly and current smoking status were found to be statistically significant predictive factors in the

development of IHD. The odds of history of HTN and current smoking were almost twice in persons with IHD compared with without (AOR=I.88, and 1.85, respectively) whereas reporting of not performing exercise regularly was twice as higher (AOR=2.09). The odds of reporting duration of diabetes for more than 5 years were doubled (AOR=1.94) within the CVA group as compared to those without CVA. Male sex, duration of diabetes for more than 5 years and current smoking status were found to be significant factors affecting the development of DF. The odds of a person with DF being male and having a duration of diabetes for more than 5 years were more than three times that of persons with no DF while history of current smoking was four times higher.

Discussion

In South Asians Association Regional Corporation (SAARC) population, there is generally a male preponderance for Type 2 diabetes, that compares with a male-female ratio of 1:1 in developing countries as a w and contrast with developed countries, where Type 2 diabetes is 1.5 times more common in women than in men.4 1 study, there was an overall predominance of females (59%).
It is well recognized that the economic status associated with the type of health facility chosen for with lower socio-economic status individuals turning to the public sector health care facilities. Males as ea members and because of cultural norms, have a relatively advantageous position in our society and chose to utilize best treatment options available, which are believed to in private clinics. 19 Significantly, more females in the utilized services from the public sector diabetes clinic and NGO diabetes clinic 69% ($p<0.001$). In the public sector/NGO diabetes clinics over half (-54%) of respondents were illiterate in the private clinic, only 8% of subjects were illiterate Amongst the illiterates over three-fourth were female the gender difference was highly significant statistically ($p<0.001$). Population based cross-sectional surveys con in a number of Asian countries, 20-22 including Pakistan 1-3,12 have shown that the prevalence of diabetes a complications increase with advancing age. This was also observed in our study, where over 65% of people were > 50 years of age. The duration of diabetes is considered an important factor in the development of complications. 6,23,24 population-based cross-sectional study in Pakistan highest prevalence of macrovascular complication found in persons having diabetes for more than 13 years. 12 About 60% of respondents in our study had diabetes more than 5 years and also a higher likelihood of developing CVA and DF. Studies have shown that obesity/overweight and lack of physical activity playa significant role in the development of diabetes 20,25 and modification of these factors substantially decreases the risk of morbidity and mortality among persons with diabetes. 15,26 In our study, 68% of people with diabetes had a BMI of > 25, majority of them (65%) were females. This is consistent with the population based diabetes surveys where females had a higher frequency of obesity. 1-3 Only a third of persons with diabetes in the study reported regular exercise (40% males vs 26% females). Performing regular exercise especially among females is not customary in our society. Smoking, although well documented as a contributing factor for the development of cardiovascular disease l4 , was found in only 8% of subjects in our study. In Pakistan, smoking is more prevalent in males (29%) as compared to females (3.4%). 19 One possible reason for an overall lower smoking rate in the study is that the study population consisted predominantly of females.

In National Health Survey of Pakistan, overall, 18% of adults were found to be hypertensive. 19 According to a cross-sectional survey in Sindh province, approximately one-half of persons with diabetes also had HTN . 1 In another study from Baluchistan province, one third of women and one fourth of men with diabetes were shown to have concurrent HTN . 2 We documented that over 42% of persons with Type 2 diabetes have HTN. Hypertension is a well- recognized factor associated with the development of cardiovascular and cerebrovascular diseases, and this risk increases further when it is associated with diabetes. 8,14 Results from landmark intervention studies demonstrate that the complications of diabetes can be prevented or delayed by controlling HTN. 16.17,27 South Asians have higher prevalence of coronary heart disease than Europeans 28.29 and other Asians. 30 The excess cardiovascular risk has not been explained by any conventional factor, such as obesity or smoking; 28 however there might be certain genetic factors responsible for this difference. A study from Sri Lanka has shown that in persons with Type 2 diabetes seen by primary care practitioners, 21% had CHD and 5.6% had stroke. 23 In our study, 26.4% had IHD and 6.8% had CVA. The prevalence of these complications are slightly higher than found in an earlier study conducted in primary care centers in Rawalpindhi (IHD 19.8% and CVA 6.2%). 12 This most likely reflects the fact that our study was conducted in specialized diabetes clinics where relatively more patients having more advanced form of diseases or referred patients are seen. Very low frequency of DF (3.9%) was documented in our study as indicated in other studies from south Asia, 12,23 in comparison to the western countries where it affects around 15% of peoples with diabetes. 31,32 The exact reason for this huge difference is still unknown. However, it is thought that it may be due to a lesssusceptibility to peripheral vascular disease in Indo-Asian population 33 and/or certain genetic factors that may be protective in nature. In addition, certain religious practices makes it obligatory to wash feet before offering prayers among Muslims and Hindus, which might serve to minimize the risk of foot infections and early detection of any problem. A recent study from India has shown that people with low-income group had a lower prevalence of diabetes; however, they have a higher prevalence of cardiac disease, neuropathy and catract. 34 The higher frequency of IHO in clinic A (with higher income group) as compared to clinics B and C is in variation with the Indian survey. On the other hand, frequencies of CYA and OF were higher in clinics B and C comprising subjects with relatively lower socio- economic group, however this difference was not statistically significant across the clinics. In multivariate analysis, hypertension, current smoking and not exercising regularly were associated with IHO; duration of diabetes more than 5 years with CVA and male sex, duration of diabetes more than 5 years and current smoking with DF. Some of the limitations in this study need to be noted. Though the data was collected from different diabetes clinics, that represent private, NGO and public sectors, the results cannot be generalized to the population of Karachi as a whole, as the study was conducted in clinics specifically focusing on diabetes.

Recommendations

A large number of persons with Type 2 diabetes in this study were suffering from macrovascular complications and had modifiable factors. Taking into account the literature review, now reinforced by the results of this study, it is strongly suggested that

every effort should be made to modify and correct any associated factor such as unhealthy dietary habits, physical inactivity, obesity, smoking habits and hypertension and thus to prevent and delay long term consequences of diabetes. Diabetes as a rapidly growing public health problem needs conscious effort and action while the pandemic is still in an early phase, both clinically and epidemiologically, through attention to health promotion, and primary and secondary prevention. Planning/delivering preventive services aiming at early detection and modification of the associated factors for the development of diabetes complications remains the best available option to deal with this huge problem. More local research is required to obtain further information regarding the disease as it behaves in our population, its risk factors and complications. Studies are needed of the most effective use of health care personnel in diabetes care at primary, secondary and tertiary levels. Information is also needed to guide the location of diabetes within integrated non-communicable disease programs at all levels of care.

Acknowledgements

We are very much indebted to Dr. Masood Kadir (Assistant Professor, Head Division of Public Health Practices and Director for Community Medicine Residency Program at Aga Khan University) for his support throughout. We are grateful to Drs. Ghulam Shabir Lakho and Nadya Khan Khuwaja for helping in data collection and data editing. We also thank Drs. Waqar Ahmed, Asad Afridi, Hafsa Raheel and Shahla Aziz (Community Medicine Residence at Aga Khan University) for helping in data collection. We also thank Bilal Iqbal (Senior Research Fellow, Department of CHS, Aga Khan University), for his helpful review of the manuscript.

References

1. Shera AS. Rafique G, Khawaja IA, et al. Pakistan National Diabetes Survey prevalence of glucose intolerance and associated factors in Shikarpur, Sindh Province. Diabet Med 1995;121116-21.
2. Shera AS, Rafique G, Khawaja 1A, et al Pakistan National Diabetes Survey prevalence of glucose intolerance and associated factors in Baluchistan Province. Diabetes Res Clin Pract 1999;4449-58.
3. Shera AS, Rafique G, Khawaja AI, et al Pakistan National Diabetes Survey Prevalence of glucose intolerance and associated factors in North West Frontier Province (NWFP) of Pakistan. J Pak Med Assoc 1999;49.206-10.
4. White F. Rafique G Diabetes prevalence and projections in South Asia Lancet 2002;360.804-5.
5. King H, Altbel1 RE, Hennan WH. Global burden of diabetes, 1995-2025 Prevalence. numerical, and projections Diabetes Care 1998;211414-31.
6. Knuiman MW, Welbom TA, McCann VJ, et al. Prevalence of diabetic complications in relation to risk factors. Diabetes 1986;35.1332-9.
7. United Kingdom Prospective Diabetes Study Group A nine-year update of a randomized, controlled trial on the effect of improved metabolic control on complications in non-insulin dependent diabetes mellitus (UKPDS 17). Ann Inter Med 1996;124136-45.
8. Spanheimer RG Reducing cardiovascular risk in diabetes Postgrad Med 2001;10926-

36.
9. World Health Organization The cost of diabetes Fact Sheet No.236. Revised September 2002 Assessed I November 2002 http://www.who/i nt/mediacentre/factsheet/fs236/en .
10. Caro JJ, Ward AJ, Judith A et al Lifetime costs of complications resulting from type 2 diabetes in U.S Diabetes Care 2002;25478-81.
11. Nicolucci A, Carinci F, Ciampi A Stratifying patients at risk of diabetic complications an integrated look at clinical, socioeconomic and care-related factors Diabetes Care 1998;211439-44.
12, Hashim R, Khan FA, Khan DA, et al Prevalence of macrovascular complications in Diabetics of WAH, District Rawalpindi J Pak Med Assoc 1999:498-11.
13. Wannamettee SG, Shaper AG, Alberti KG Physical activity, metabolic factors and the incidence of coronary heart diseases and type 2 diabetes Arch Intern Med 2000;1602108-16.
14. Multiple Risk Factors Intervention Trial Research Group Diabetes, other risk factors and 12 year cardiovascular mortality for men screened in the multiple risk factor intervention trial Diabetes Care 1993;16434-44.
15. Williamson DE, Thompson TJ, Thun M, et al 1ntentional weight loss and mortality among overweight individuals with diabetes Diabetes Care 2000;231499-1504.
16. United Kingdom Prospective Diabetes Sl1ldy Group Tight blood pressure control and risk ofmacrovascular and microvascular complications in type 2 diabetes (UKPDS 38) BMJ 1998;31n03-713.
17. United Kingdom Prospective Diabetes Study Group Association of systolic blood pressure with macrovascular and microvascular complications of type 2 diabetes (UKPDS 36) BMJ 2000;321 412-19.
18. Bureau of Statistics, Government of Sind, Pakistan Population Census 1998.
19. Pakistan Medical Research Council National Health Survey of Pakistan 1990-94, Islamabad, Pakistan Network Publication Services, 1998.
20. The National Diabetes Prevention and Control Cooperative Group Prevalence of diabetes and its risk factors in China, 1994 Diabetes Care 201997;1664-68.
21. Sayeed MA, Ali L, Hussain MZ, et al Effects of socioeconomic risk factors on the difference in the prevalence of diabetes between rural and urban population in Bangladesh, Diabetes Care 1997;20551-55.
22. Diabetes Epidemiolol,'Y Study Group in 1ndia (DESI) High prevalence of diabetes and impaired glucose tolerance in India National Urban Diabetes Survey, Diabetologia 2001:441094-1101.
23. Weerasuriya N, Siribaddana S, Dissanayake A, et al Long-term complications in newly diagnosed Sri Lankan patients with type 2 diabetes mellitus Q J Med 1998;91'439-43.
24. The S1D-AMD Italian Study Group for the Implementation of the St Vincent Declaratiow a comprehensive assessment of the avoidability of long term complications of diabetes, Diabetes Care 1996;19'927-33.
25. Wing RR, Venditti E, Jakicic JM, et al Lifestyle intervention in overweight individuals with a family history of diabetes Diabetes Care 1998;21350-59.
26. Hu FB, Stampfer MJ, Solomon C, et al Physical activity and risk for cardiovascular events in diabetic women Ann Intern Med 200 I ;3496-105.

27. Hypertension Optimal Treatment Study Group Effects of intensive blood pressure lowering and low dose aspirin in patients with hypertensiow principal results of the hypertension optimal treatment (HOT) randomized trial Lancet 1998:3511755-62.
28. McKeigue PM, Ferrie JE, Pierpoint T, et al Association of early onset coronary heart disease in south Asian men with glucose intolerance and hyperinsulinemia, Circulation 1993;87' 152-61.
29. Chowdhury TA, Lasker SS Complications and cardiovascular risk factors in south Asians and Europeans with early-onset type 2 diabetes Q J Med 2002;95'241-6.
30. Lee J, Heng D, Chia KS, et al Risk factors and incident coronary heart disease in Chinese, Malay and Asian Indian males the Singapore Cardiovascular Cohort Study Int J Epidemiol 2001 :30983-8.
31. Morgan CL, Currie CJ, Stott NC, et al The prevalence of multiple diabetes related complications, Diabet Med 2000;17'146-51.
32. Bloomgarden ZT American Diabetes Association 60th scientific session, 2000, Diabetes Care 2001 ;24 946-51.
33. Burden AC Diabetes in Indo-Asia!l people Practitioner 2001 ;245445-52.
34. Ramachandran A, Snehalatha C, Vijay V, et al 1mpact of poverty on the revalence of diabetes and its complications in urban southern India, Diabet Med 2002;19:130-35.