Prevalence of Chronic Complications and Associated Factors in Type 2 Diabetes

A. S. Shera, F. Jawad, A. Maqsood, S. Jamal, M. Azfar (Diabetic Association of Pakistan and WHO Collaborating Centre for Diabetes, Karachi.)
U. Ahmed (Diabetic Association of Pakistan and WHO Collaborating Centre for Diabetes, Karachi.)

Abstract

Objective: To determine the prevalence of chronic complications and associated factors in type 2 diabetes in 500 diabetic patients, age ≥ 25 years, attending the clinic of Diabetic Association of Pakistan (DAP), Karachi.

Methods: Every 5th registered diabetic patient ≥ 25 years age, was examined for the presence/absence of micro and macro vascular complications and associated factors. Blood samples were collected for HbA1c, lipid profile and serum creatinine. Urine was examined for albumin and microalbumin.

Results: Of the 500 diabetic patients examined (160 males, 340 females, mean age 55.2 ± 10.6 years), retinopathy was seen in 43%, neuropathy in 39.6% and foot ulcers in 4%. Nephropathy was found in 20.2%, and was significantly associated with hypertension. The prevalence of microvascular complications was higher in the group of patients with HbA1c >8% and was significantly related to duration of diabetes, hypertension and obesity. Hypertension was manifest in 64.6% patients, 61% had raised Body Mass Index and Waist Hip Ratio was more than normal in 88% subjects. Macrovascular complications were encountered in 102 diabetic patients, with angina in 85 (17%), heart attack in 25 (5%) and stroke in 13 (2.6%).

Conclusion: The prevalence of diabetic microvascular complications was higher in people with poor glycaemic control, longer duration of diabetes and associated hypertension and obesity (JPMA 54:54;2004).

Introduction

The development and progression of chronic complications of diabetes are closely related to glycaemic control. Micro and macrovascular pathological lesions can involve various organs and tissues resulting in significant morbidity and mortality. Studies have shown Diabetic Nephropathy to be the leading cause of End Stage Renal Disease (ESRD). Data collected by USRDS in 200 Ion ESRD including diabetic nephropathy, has shown that the incidence rates of treated ESRD have risen world wide. The prevalence rates are increasing also, with the highest being in Japan, Taiwan and USA (1400-1640 pmp) and the lowest in Pakistan and Bangladesh (48-58 pmp). Similarly Diabetic Retinopathy is an important cause of blindness. Management and treatment of diabetic complications imposes a significant economic burden on the state and the individual. In addition, complications of diabetes have a considerable impact on the quality of life of the patient. It, therefore, becomes imperative to institute effective screening and preventive strategies to detect the early signs of complications. The development of complications of diabetes varies among different ethnic groups. The frequency of ESRD in Type 2 diabetes is four fold higher in black and native American population compared to the white people.
Several studies from India, including a series of 3010 cases, showed a high prevalence of vascular complications in Type 2 diabetes. A comprehensive study from Pakistan on 1000 people with diabetes, reported high figures of complications. This along with high prevalence of Type 2 diabetes in the country, emphasizes the need for adoption of strict measures for prevention and early detection of diabetes. This study was undertaken to determine the prevalence of retinopathy, nephropathy, neuropathy, coronary artery disease, cerebrovascular disease and associated factors i.e., obesity and hypertension, in Type 2 diabetic patients.

Patients and Methods

Type 2 diabetic patients > 25 years of age presenting to the outpatient clinic of the Diabetic Association of Pakistan (DAP) Karachi, were studied. DAP is a charitable organization located in Karachi, the largest city of Pakistan, with a population of 12 million. This facility provides laboratory services along with consultation by trained doctors at nominal rate. Charges are reduced or waived for individuals unable to pay the amount. The patients are mostly self referred and represent all social and demographic strata in Karachi. A large majority belongs to the low and middle socio-economic class. A random sample of every fifth, previously registered type 2 diabetic patient age > 25 years, presenting for routine follow up, was selected after informed consent. Subjects with urinary tract infection, detected by dipstick (multistix), pregnant diabetic women, individuals with a protuberant belly or umbilical hernia and those who did not consent to participate, were excluded. In the above instances, the subsequent patient was included. Doctors familiar with the protocol interviewed all the selected subjects and answers were noted on a coded structured proforma. Demographic details, family history of diabetes, lifestyle details, medical and treatment history with specific reference to hypertension, coronary artery disease, cerebrovascular accident and foot ulcers were documented. Height and weight were recorded for body mass index (BMI-weight in kg/height in m^2). BMI between 18.5 and 24.9 was considered normal, >25.0-26.9 as overweight. Waist hip ratio (WHR) was calculated by the formula, waist girth in cm/hip girth in cm. The normal figure for males was < 0.95 and for females < 0.85. Hypertension was defined as the presence of systolic BP >140 mm Hg and diastolic BP of >90 mmHg or a known hypertensive on treatment. Femoral, popliteal, tibialis posterior and dorsalis pedis arteries were palpated and noted as normal, diminished, absent or leg amputated. Sensation was examined using a 10-gram Semmes- Weinstein monofilament on the ten recommended sites on plantar and dorsal aspects of feet. The results were documented as normal, diminished, absent or leg amputated. Subjects with diminished or absent sensation were labelled as neuropathic. The knee and ankle reflexes were elicited and noted as normal, diminished, absent or leg amputated. Subjects with diminished or absent knee or ankle reflex or amputation on either limb were labelled as neuropathic. Feet were examined for the presence of callus, healed ulcer or active ulcer. Fundal examination was performed by indirect ophthalmoscopy. Microdots, blot haemorrhages and hard and soft exudates were considered as background retinopathy. The presence of new vessels was taken as proliferative retinopathy. Macrovascular complications were defined as history positive for one or more of three conditions: angina, heart attack or stroke. Biochemical Tests All subjects were asked to come for blood sample collection in the morning after an
overnight fast of 10 -14 hours. They were also advised to bring the first morning sample of urine in a supplied container, for examination including microalbumin estimation. Microalbumin was estimated by MICRAL TEST on Accu-check product, Roche Diagnostics GmbH, Mannheim Germany. Serum total cholesterol, triglyceride, HDL, LDL cholesterol, serum creatinine and glycosylated haemoglobin (Bio-Rad DiaSTAT Hemoglobin A1c Program Bio-Rad Laboratories CA USA) (normal range for people without diabetes 4.4-6.4%) were estimated. Cholesterol levels <200mg/dl were considered normal, 200 -250 as increased risk and >250 as high risk, triglyceride levels <150 mg/dl were defined as normal, 150 -200 as increased risk and > 200 as high risk. HDL levels >40 mg/dl were taken as normal, 30 -40 as increased risk and <30 as high risk. HbA1c of <7% was considered as good glycaemic control, 7-8% acceptable and >8% poor control. Nephropathy was defined as presence of protein either macroalbumin or microalbumin and absence of pus cells in urine. The creatinine level <1.2 mg/dl was taken as normal. Statistical methods All data was analyzed by with statistical package "SPSS version 10.0". The participants were placed in four categories, according to the duration of diabetes: 0-5, 5-10; 10-15 and = 15 years. Age was divided in four quartiles: 25- 47,47-55, 55-63, >63 years. Age, sex, duration of diabetes, BMI, WHR and HbA1c were tested individually as independent variables against the specified complications. Moreover, these specified complications were also tested against each other. The results for continuous variables are given in the form of averages, standard deviations (S.D.) and 95% confidence intervals (C.I.). The odds ratio (OR) and X² values were calculated to find the association among categorical variables.

Results

The study included 500 people with Type 2 diabetes, (160 males, 340 females) with a mean age of 55.2±10.6 (range 25-85) years. The median duration of diabetes was 7 years following diagnosis. The duration of diabetes against the number of subjects is shown in Figure. WHR and BMI greater than normal were noted in 87% and 61% individuals respectively. Cholesterol and triglyceride levels were raised in 46% and 49% diabetic patients respectively and 80% had less than normal HDL. Microalbuminuria was present in 13%. Of the 323 (64.6%) people with hypertension, 225 (69.7%) gave a history of previously diagnose hypertension, and 156 (48.3%) were on anti hypertensiy medication. Newly diagnosed hypertension was found in 9 (19.6%) subjects. HbA1c level >8% was present in 142(28.4%), 7-8% in 89 (17.8%) and <7 in 269 (53.8% Retinopathy (43%) was the most frequent complication, followed by neuropathy (39.6%), nephropathy (20.2%) an foot ulcer (4%). One hundred and two subjects were found to hay one or more than one of the macrovascular complication angina 85 (17%), heart attack 25 (5%) and stroke 13 (2.6%). In the univariate analysis, neuropathy was found be significantly associated with duration of diabet (p=0.001), BMI (p=0.04), trophic ulcer (p=O.02 nephropathy (p=0.001) and HbA1C (p=0.02). Nephropathy showed significant association with HbA1c (p=0.001 duration of diabetes (p=0.05) and hypertension (p=O.05) Similarly, retinopathy was found to be associated wit duration of diabetes (p=0.001) and trophic ulcer (p=O.OOI) A significant association was also observed between hypertension and WHR (p=O.O 1 ). All complications, except trophic ulcer, showed significant association with age, nephropathy (p=0.04), neuropathy (p=0.001 ),...
hypertension (p=0.001), and retinopathy (p=0.001). Gender had no association with any microvascular complication. Macrovascular complications showed significant association with duration of diabetes (p=0.001), gender (p=0.001) and age (p=0.04). No difference was found between people with normal and high cholesterol levels with respect to duration of diabetes, hypertension, BMI and WHR. Similarly, there was no association between any of the above-mentioned variables and triglyceride levels. The multivariate analyses of different risk factors are shown in Tables I and 2. In logistic regression analysis, a significant association of nephropathy was found with HbA1c (Adjusted OR=2.1, 95% C.I.: 1.3-3.9), hypertension (Adjusted OR=4.1, 95% C.I.: 2.2-7.7), and retinopathy (Adjusted OR=3.7, 95% C.I.: 2.1-6.4). Additionally, hypertension was found to be associated with nephropathy (Adjusted OR=4.5, 95% C.I.: 2.4-8.3) and WHR (Adjusted OR=2.0, 95% C.I.: 1.04-3.8). Similarly, retinopathy was found to be significantly associated with nephropathy (Adjusted OR=1.9, 95% C.I.: 1.2-2.9), nephropathy (Adjusted OR=3.4, 95% C.I.: 1.98-5.8), presence of ulcer (Adjusted OR=3.4, 95% C.I.: 1.02-11.5) and Duration of diabetes (Adjusted OR=5.6, 95% C.I. 2.8-11.3). Retinopathy was also associated with increasing categories of duration with adjusted odds increasing from category 5-10: 2.8 (95% C.I.: 1.65-4.9) to category 15 or more: 5.6 (95% C.I: 2.8-11.3). Neuropathy was found to be associated with gender (Adjusted OR=1.9, 95% C.I. 1.2-2.9) and HbA1C (>7%) (Table 1). Macrovascular complications also showed significant association with duration of diabetes, with strength of association rising from Adjusted OR=0.99, 95% C.I.: 0.5-1.9 to Adjusted OR=3.0, 95% C.I.: 1.5-6.0) as the duration increased from 0-5 years to > 15 years respectively. Macrovascular complications were also significantly associated with gender (Adjusted OR=2.3, 95% C.I.: 1.4-3.7) and BMI (Adjusted OR=2.1, 95% C.I.: 1.2-3.5) (Table 2).

Discussion

The UK prospective diabetes study (UKPDS) proved that in patients with type 2 diabetes the risk of complications was strongly associated with previous hyperglycaemia. Any reduction in HbA1c is likely to reduce the risk of complications, with the lowest risk being in those with HbA1c values in the normal range (<6.0%). In Pakistan, with a population of 140 million, has a diabetes prevalence of 11.4% in the age group 25 years and above. No countrywide survey on diabetic complications has been conducted so far. Keeping in view the high prevalence of Type 2 diabetes, the number of people with chronic complications is likely to be high. Our results could be biased, as in the DAP clinic doctors trained in diabetes care attend to the patients. It is therefore possible that the risk of developing chronic complications in these patients may be less as compared to those receiving treatment from General Practitioners, who have less time and lesser experience to provide treatment, motivation and encouragement. Female preponderance (340 F: 160 M) in our study has also been observed in the Pakistan National Diabetes Survey conducted by DAP. Most men belonging to low-income group, were daily wage earners and found it difficult to attend the clinic regularly, while most women were housewives and came to the clinic when advised. Retinopathy: This was more commonly seen in our series (43%) compared to the prevalence of 23.7% reported in the Indian study. A group from Egypt has reported retinopathy in 42% of their study subjects which closely matches our findings. A publication from Cardiff UK from a district
health authority population found retinopathy to be present in 16.5% diabetic patients, whereas a Spanish study gave figures of 30.6% retinopathy in 504 people with type 2 DM. The results on 503 Mexican people with type 2 DM revealed 44.6% retinopathy. The high figures of retinopathy in our population could be attributed to a lack of awareness in our patients to undertake regular eye examination. A genetic factor may also be relevant, as the figures between the UK subjects and those from Mexico, Egypt and Pakistan show significant disparity. Neuropathy: Neuropathy is often ignored due to insidious onset and slow progress. This could be the reason for our figure of 39.6%, which is higher than the Indian results (27.5%). Significant association between neuropathy, retinopathy and glycaemic control was noted. A multicentre Italian study showed 32.3% subjects to have diabetic neuropathy, whereas the prevalence of neuropathy was quoted as 38% from Saudi Arabia. Each study had results with a significant association with the duration of diabetes. Several studies have shown that foot ulcers, both ischemic or neuropathic, have a low prevalence in South Asians. A EURODIAB population based case controlled study done in UK concluded that South Asians with diabetes have 25% lesser risk of amputation compared to Europeans. This is attributed to the low rates of PVD and neuropathy in the former. Our study gave a figure of 4% ulcer prevalence with only one case with a digit amputation. A study from Saudi Arabia, reported 4.7% foot ulcers and 3.4% below ankle amputations. Contributing factors for the low prevalence of foot complications in South Asians and Middle Eastern population, could be differences in footwear design (sandals), increased attention to foot hygiene due to cultural practices of 'wudu', the ablution required of Muslims before prayer which involves washing the parts of the body that are generally exposed to grime and dust. This practice allows inspection and cleaning of the feet five times daily. A genetic factor may also play a role. Diabetic Nephropathy: DN is the leading cause of ESRD in Japan, Taiwan and the United States. Infection remains the leading cause for ESRD in developing countries, followed by diabetes. A study from Pakistan has shown similar results. It has been observed that ethnicity and racial differences play a major role in the development of DN. Black Americans and Pima Indians have a higher prevalence of DN compared to the whites. Macroproteinuria and microalbuminuria has been reported to be higher in British Asians than in the white population. A study from Saudi Arabia reports a rapid progression of diabetic kidney disease in their patients with 12 out of 24 becoming dialysis dependent within 19.7 months. Another clinic based study from Riyadh reports 41.3% diabetics having microalbuminuria and 12.7% clinical nephropathy (albustix positive). Both were related to poor glycaemic control and obesity. Figures from an Indian study on 3010 subjects (mean age 52 + 9.7 years) quote 19.7% subjects having proteinuria. Of these 5.5% had persistent proteinuria > 500 mg/dl. Our study results show that 20.2% of the subjects had DN, with significant association with age, level of glycaemia, duration of diabetes, hypertension and obesity. Other studies, including the UKPDS, have shown similar association. UKPDS has demonstrated that intensive control of blood glucose reduces the risk of early kidney damage by 33%. Coronary Artery Disease and Cerebrovascular Disease: An Indian publication found 11.4% subjects to have CAD and 0.9% with a past history of stroke, as compared to 20.4% and 2.6% respectively in our series and 25.2% and 9.6% respectively in a UK study. Earlier data on South Asian immigrants in UK also showed a high prevalence. CAD was found to be significantly associated with female
gender in our study. Hypertension and obesity, important risk factors for CAD, were also present more frequently in women. The Strong Heart Study 29 and other studies also suggest that the relative risk of CAD in women with diabetes is independent of the conventional risk factors. 30 Obesity is a major contributing factor to non-communicable diseases. The prevalence of obesity seen in most Pakistani studies has been high, similar to our results of 87% with above normal WHR(>0.85 females, >0.95 males) and 61% with a raised BMI(>27kg/m2). Haider et al reported 56% of 500 subjects with essential hypertension to be obese as measured by the Ponderal Index. 31 In a survey on the prevalence hypertension and obesity in 151 women over 25 y age belonging to a low income area of Karachi, 4i were overweight and 8% were obese according to (overweight: BMI 23-29, obese: BMI >29). 32 Jabbar et al in their study on dyslipidaemia an relation with BMI versus WHR on 88 subjects, me age 41 years, concluded that total cholesterol significantly higher in men and women with a WHR more than 0.9 and 0.8. High BMI did not show association. This emphasizes the importance of rou measurement of WHR. 33 The Pakistan National Diabetes Survey confirmed the strong association between glucose intolerance WHR above the normal range. 6 The association of obesity with diabetes, cardiovascular disease and hypertension has b reported from allover the world. For Asian population, there is perhaps a need for lower BMI indices as cut levels for obesity. Women tend to have higher obe rates than men and obesity is now emerging as a factor even in the poor population of the develo countries. 34 Hypertension was present in 323 (64.6%) subjects. This is a higher figure compared to the results of Pakis National Prevalence Survey (37%) 5,8,9 and publication’ from India and Bahrain 3,35 , each showing 38%. It was observed that 94% of subjects with a raised WHR 47.4% with high BMI had hypertension. The prevalence of hypertension in our patients could attributed to central obesity and cultural habits of salt intake. Our study concluded that the prevalence of diabetic microvascular complications was higher in people poor glycaemic control, longer duration of diabetes associated hypertension and obesity. We recommend screening of high risk groups and emphasize importance of early diagnosis of diabetes and detection chronic complications so that appropriate treatment initiated at the earliest.

Acknowledgements

The study was funded by WHO. The statistical analysis by Dr. Agha Ajmal is gratefully acknowledged.

Annoucement

The 5th Diabetes in Asia Conference, will be held under the aegis of Diabetic Association of Pakistan, Karachi and International Diabetes Federation, from 16 to 18 April 2004, in Karachi. The theme of the conference is "Prevention of Diabetes." The conference will be addressed by 30 foreign delegates, experts in Diabetes, along with President IDF Prof. Pierre Lefebvre. Local data will be presented by doctors from all the provinces. Details can be had from Diabetic Association of Pakistan & WHO Collaborating Centre, Karachi, telephone: 92-21- 6616890, fax: 92-21-6680959, email: dapkhi@cyber.net.pk, web site: www.dap.org.pk
References

2. Klein R Hyperglycemia and microvascular and macrovascular di diabetes Diabetes Care I 995; I 8258-68.
South Asians vs Europeans in the UK Diabet Med 2002;1999-104.