# Causes of Death and Prognostic Factors of NIDDM Patients

## 1. Introduction

Many studies have found that the mortality of NIDDM (non-insulin-dependent diabetes mellitus) patients is 2-6 times higher than that of the general population [1-3]. This higher mortality is considered to be due to the higher prevalence rates of cardiovascular diseases, diabetes, cerebrovascular diseases, renal diseases and malignant neoplasms among diabetes patients [4, 5]. Since 1993, diabetes has been the fifth leading cause of death in Taiwan. It is also a chronic disease of significantly increasing mortality [6]. Although NIDDM is a serious public health problem in Taiwan, very little has been done to study it. The present study is to understand the conditions of NIDDM patients and their pregnostic factors.

## 2. Study Design and Method

Data collection

The retrospective cohort study method was applied to collect information from patients who were diagnosed NIDDM at a teaching hospital in the period between March 1989 and June 1994. Their medical records were reviewed and information concerning their demographic characteristics, blood pressure and laboratory findings of some biochemical values such as blood sugar at fasting, cholesterol, triglyceride, high density cholesterol, and protein urine were collected.

### Definition

The WHO criteria for diabetes were used: blood sugar at fasting larger than or equal to 7.8 mmol/L (140 mg/dl), or blood sugar after oral glucose tolerance test larger than or

equal to 11.1 mmol/L (200 mg/dl)[7].

Hypercholesterolemia is defined as serum cholesterol larger than or equal to 200 ml/dl. Hypertriglyceridemia is defined as triglyceride larger than or equal to 200 mg/dl. A hyperlipidemia case is one who has taken antihyperlipidemia medicine, or his serum cholesterol larger than or equal to 200 mg/dl, or triglyceride larger than or equal to 200 mg/dl.

Obesity is defined as one whose BMI (body mass index) is larger than or equal to 27 for men and 25 for women [9].

A hypertensive case is defined as one who has taken anti-hypertension medicine, or whose systolic pressure is higher than 160 mmHg, or diastolic pressure higher than 95 mmHg. Blood pressure under 140/90 mmHg is normal; that between the two is defined as borderline [10].

Survey

In addition to data collection, interviewers also collected information through a structured questionnaire from family members of patients. Data collection was completed in June 1994. Items in the questionnaire included: demographic data, personal and family health history; if already dead, date of death and cause of death. The direct cause of death registered on the vital statistics by the Taiwan Provincial Health Department was used in the analysis of cause of death. The survival time was the time between the diagnosis of diabetes and 30 June 1994. For the deceased, the survival time was the time between the diagnosis of diabetes and the time of death.

Statistical analysis

Data were analyzed with Epi-Info and SAS. $\chi^2$ test was used to test the risk factors of death. Cox's proportional hazard regression model was used for multi-variate analysis to study the impact of each risk factor on the survival of patients.

## 3. Results

Hospital care and cause of death

766 hospitalized NIDDM patients were studied. Their average age was 64 yr $\pm$ 11.8; and there were more women than men (424 vs 342). They were first time admitted to hospital for cardiovascular diseases (23.9%), high blood sugar (23.4%), retinopathy (20.4%) and renal diseases (14.6%) (Table 1). Median time of follow-up was 3.5 year (range 1 month to 4.6 yr). 131 (59 males and 71 females) had died and 635 were still alive. The direct causes of death of these 131 patients were: cardiovascular diseases (34.9%), diabetes (16.3%), renal diseases (9.4%), pneumonia (7.0%) and cerebrovascular diseases (6.9%) (Table 2). Death certificates were issued by hospitals

(88.6%), forensic

**Table 1. NIDDM Patients Under Hospital Care of First Time by Cause, 1989-1994**

| Cause of Hospital Care | % |
|---|---|
| Cardiovascular diseases | 23.9 |
| Hypertension | 23.4 |
| Retinal disorders | 20.4 |
| Renal diseases | 14.6 |
| Infections | 4.4 |
| Coma | 2.6 |
| Hypoglycemia | 1.4 |
| Cerebrovascular diseases | 1.2 |
| Pneumonia | 0.5 |
| Others | 7.6 |
| Total | 100.0 |

**Table 2. Direct Causes of Death of NIDDM Patients, 1989-1994**

| Direct Cause of Death | % |
|---|---|
| Cardiovascular diseases | 34.9 |
| Diabetes | 16.3 |
| Renal diseases | 9.4 |
| Pneumonia | 7.0 |
| Cerebrovascular diseases | 6.9 |
| Cancers | 3.9 |
| Infections | 2.3 |
| Unknown reasons | 18.6 |
| Total | 100.0 |

medicine doctors (4.9%), clinics (3.3%) and others (2.2%). 33% of the death certificates did not mention diabetes as the cause of death.

Prognostic factors of NIDDM deaths

Table 3 shows the predictive factors of NIDDM deaths and survivals. Death rate from all causes of those with blood sugar at fasting larger than or equal to 260 mg/100 dl was 2.6 times higher than those of blood sugar at fasting smaller than 260 mg/100 dl (95% confidence interval at 1.5-4.4). Death rate from all causes of those with albuminuria was 2.2 times higher than those without (95% confidence interval at 1.4-3.4). Patients of longer diabetes history tended to have higher risk of death ($p<0.0l$). Age at first diagnosis of diabetes was positively correlated to death rate from all causes ($p <0.01$). That is, when diabetes was diagnosed at later ages, chances of death were higher. Death rate from all causes of those with both parents of diabetes history was 0.35% higher than those without (95% confidence interval at 0.15-0.79).

BMI, serum cholesterol, serum triglyceride and hypertension were not found statistically to be significantly related to the death risks of NIDDM.

When all factors at $p<0.05$, BMI and hypertension were analyzed under the Cox's proportional hazard model, it was found that blood sugar at fasting, BMI and age at first diagnosis of diabetes were significantly related to the survival time. That is, the earlier the diagnosis was made, the smaller the BMI value was, and the lower the blood sugar at fasting was, the longer the survival time would be (Table 4).

## 4. Discussion

The subjects studied were hospitalized patients. They would have more complications, their chances of survivals, therefore, would be poorer [11]. However, the finding of the present study that hospitalized diabetes patients had higher mortality than the general population corresponded to the similar finding using the population-based diabetic patients [4]. This is perhaps due to the fact that after the appearance of insulin, diabetic patients receive better treatment, their health conditions have thus improved. Entmacher et al [1] reported that since 1930, the mortality of the diabetic patients treated at the Joslin Clinic had significantly declined, their survival rate had also improved.

The present study showed that the direct cause of death of NIDDM patients was cardiovascular diseases, to be followed by diabetes. This finding was similar to findings of other studies [4, 5]. Cardio-vascular diseases are major complications of NIDDM patients.

Some studies mention that the younger the diabetic patients' age is, the higher the mortality will be. This finding is not the same as the finding of the present study. This might have to do with the care environment the patients were in [12]. The present study found that the relative risk of death of those diagnosed earlier was lower. Early

diagnosis and early treatment improved the survival rate. This finding corresponded to

Table 3. Prognostic Factors of Mortality of NIDDM Patients

| Variables | No. of Death (%) | No. of Survival (%) | Age-Sex Adjusted OR (95%CI) |
|---|---|---|---|
| Obesity: | | | |
|   Yes | 13(10.2) | 115(89.8) | 1.16(0.60-2.24) |
|   No | 59(10.4) | 509(89.6) | |
| Blood sugar at fasting: | | | |
|   >260 mg/dl | 112(20.4) | 436(79.6) | 2.58(1.52-4.40)** |
|   <260 mg/dl | 19( 8.9) | 194(91.1) | |
| Hypercholesteremia: | | | |
|   Yes | 52(15.5) | 284(84.5) | 1.07(0.69-1.65) |
|   No | 66(19.8) | 267(80.2) | |
| Hypertriglyceridemia: | | | |
|   Yes | 44(17.5) | 208(82.5) | 1.29(0.81-2.07) |
|   No | 55(16.5) | 278(83.5) | |
| Hyperlipidemia: | | | |
|   Yes | 68(13.5) | 436(86.5) | 0.57(0.38-0.87))) |
|   No | 63(24.1) | 198(75.9) | |
| Albuminuria: | | | |
|   Yes | 93(22.1) | 328(77.9) | 2.19(1.40-3.43) |
|   No | 33(10.8) | 273(89.2) | |
| Hypertension: | | | |
|   Yes | 98(19.5) | 404(80.5) | 1.62(0.97-2.71) |
|   No | 22(10.2) | 194(89.8) | |
| High density cholesterol: | | | |
|   <35 mg/ml | 7(18.4) | 31(81.6) | 2.11(0.64-6.95) |
|   >35 mg/ml | ( 8.0) | 80(92.0) | |
| Duration of diabetes: | | | |
|   <5 years | 8( 7.6) | 97(92.4) | |
|   5-10 years | 24(11.7) | 181(88.3) | 1.56(0.68-3.59) |
|   11-15 years | 28(17.3) | 134(82.7) | 2.03(0.89-4.61) |
|   16-20 years | 29(22.0) | 103(78.0) | 2.41(1.05-5.52)* |
|   >20 years | 41(27.3) | 109(72.7) | 2.70(1.21-6.00)* |
| Age at diagnosis: | | | |
|   30-39 | 7( 6.3) | 105(93.7) | |
|   40-49 | 33(16.1) | 172(83.9) | 2.9(1.2-7.4)* |
|   50-59 | 44(18.3) | 196(81.7) | 3.4(1.4-8.5)** |
|   60-69 | 35(25.7) | 101(74.3) | 5.2(2.1-13.5)** |
|   >70 | 10(23.8) | 32(76.2) | 4.7(1.5-15.1)** |

$\chi^2$-test: * $p<0.05$; ** $p<0.01$. CI=confidence interval

**Table 4. Analysis of Prognostic Factors of the Survival of NIDDM Patients by Cox Proportional Hazard Model**

| Variables | Odd Ratio (SE) | p-value |
|---|---|---|
| Age at first diagnosis | 1.036(0.004) | 0.0001 |
| BMI | 1.011(0.005) | 0.0161 |
| Blood sugar at fasting | 1.001(0.002) | 0.0002 |

Odds ratio increases by 1.036 times when the age at first diagnosis increases by one year; odds ratio increases by 1.011 times when BMI increase by 1; odds ratio increases by 1.001 times when blood sugar at fasting increases by 1 mg/dl.

the conclusion of Entmacher et al[1].

Poor control of blood sugar is the major cause of albuminuria. Albuminuria is an indicator of changes in renal functions. Whitehall [13], in his ten-year follow-up of asymptomatic high blood sugar patients, found that the discharge rate of albumin in the patients who died was higher than that in the survived patients. Long-lasting albuminuria was significantly related to the increasing risk of death of NIDDM patients [14, 15]. Nelson et al [16] found that 97% of the increase in the mortality of the NIDDM patients of the Pima Indians was related to albuminuria. The mortality of diabetic patients without albuminuria is close to that of the general population. The present study also found that albuminuria was related to the risk of death from all causes of NIDDM patients. However, in the multi-variate analysis, albuminuria was not found to be significantly related to the risk of death. This finding corresponded to that of Morrish et al [17]

Some studies mentioned that hypertension the prognostic factor of diabetes [18]. Some studies, on the other hand, mentioned that hypertension had no effect on the mortality of diabetes [19]. Data from the Diabetes Intervention Study showed that more hypertension hyperlipidemia and obesity were found on NIDDM patients, and more hypertensive NIDDM patients died of cardiovascular and cerebro-vascular diseases. Many cohort follow-up studies, however, indicated that it was the mechanism of athro-sclerosis that increased the mortality of NIDDM patients [3]. In the present study, hypertension was found to be related to the risk of death of NIDDM patients only in the uni-variate analysis; in the multi-variate analysis, hypertension was not found statistically to be related to the risk of death of NIDDM patients. This perhaps was that hypertension was a common symptom of all diabetic patients at terminal stage. 70% of the NIDDM patients in the present study had hypertension.

Obesity is one of the risk factors for the increasing mortality of diabetic patients [20,

[21]. In the multi-variate analysis, though not in the uni-variate analysis, of the present study, obesity was found to be significantly related to the risk of death of NIDDM patients. The number of cases perhaps was not sufficient in the single-variate analysis.

In general, the present study further confirmed that the following factors could increase the risk of death of diabetes patients: blood sugar at fasting, age at first diagnosis and obesity. Early diagnosis, early treatment and adequate diet control are some important measures in improving the prognosis of NIDDM patients.

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