End-stage renal disease in NIDDM: a consequence of microangiopathy alone?

A.E.G. Raine^{†1}, R. W. Bilous²

¹ The Royal Hospital of St. Bartholomew, London, UK

² Diabetes Care Centre, Middlesbrough General Hospital, Middlesbrough, UK

The number of patients developing end-stage renal disease (ESRD) due to diabetes mellitus is increasing and most of these patients have the non-insulin-dependent form (NIDDM) [1, 2]. In addition to the need for renal replacement therapy (RRT), such patients also have other diabetic complications affecting the micro- and macrovasculature. Survival, once renal failure is established, remains disappointingly low and significantly lower than for non-diabetic renal failure patients, mainly due to cardiovascular disease [3]. Although the natural history of renal complications has been well-researched in insulin-dependent (IDDM) patients, there are far fewer studies in NIDDM [4]. Similarly the pathophysiology of diabetic nephropathy has been studied primarily in IDDM. In addition, there is some question as to whether proteinuria in IDDM is diagnostic of diabetic glomerulopathy alone [5–7]. This short report will briefly discuss the present incidence and prevalence of diabetic ESRD and its changing pattern in Europe. Finally, it will comment on whether ESRD in NIDDM is due primarily to microangiopathy.

Worldwide incidence of prevalence of diabetic ESRD

True incidence and prevalence of diabetic ESRD is difficult to assess because most registry data depend upon referral to an RRT programme. Patients who are not referred because of age or other medical

complications will not, therefore, be registered. The acceptance rate of diabetic ESRD patients to RRT programmes in 1992 is shown in Table 1. The European average of 6 per million population is one tenth that of the United States, although there is a wide range both between and within individual countries. Part of this variation is a reflection of ethnic case mix. Diabetes and its complications are common in Asian patients [8] which partly explains why the acceptance rate in St. Bartholomew's Renal Unit in London is five times the national average (it is situated in an area with a high number of Asians). African-Americans also have a higher prevalence of diabetes and ESRD, and comprise a large proportion of patients on RRT in the United States [9]. Most Japanese patients with diabetes have NIDDM, but much lower rates of cardiovascular disease than their western counterparts [10]; thus, many more may survive to develop renal failure and need RRT.

The worldwide incidence of new enrolment in RRT is showing a similar trend upwards, however, with over one third of such patients in the United States [2] and one fifth in Europe [1] having diabetes as their primary cause of ESRD.

Changing patterns of IDDM and NIDDM ESRD in Europe

The European Dialysis and Transplant Association Registry (EDTA) probably has the most complete longitudinal data available on the changing patterns of referral for RRT. Over the decade 1982–1992, the increase in patient acceptance was almost exclusively in the age range 45–65 and 65+ years [1]. The increase in number of patients with diabetic ESRD is also within these age ranges and is likely to be predominantly NIDDM. Since 1983, the EDTA Registry has coded separately for IDDM and NIDDM. The

Corresponding author: Dr. R. W. Bilous, Diabetes Care Centre, Middlesbrough General Hospital, Middlesbrough, UK

Abbreviations: ESRD, End-stage renal disease; IDDM, insulin-dependent diabetes mellitus; NIDDM, non-insulin-dependent diabetes mellitus; RRT, renal replacement therapy; EDTA, European Dialysis and Transplant Association

[†] Deceased

Table 1. Acceptance of diabetic ESRD for RRT in 1992

	per million population
USA (1990)	62
Japan	50
Canada	24
EDTA	6
Austria	21
Denmark	14
Netherlands	9
London (1994) (76 % NIDDM)	34

Table 2. Why is there such disparity in reporting of non-diabetic renal disease in NIDDM?

- Small sample numbers?
- Selection bias (retrospective studies)?
- Ischaemic glomerular lesions in elderly NIDDM patients?
- True racial/geographical differences?
- Variations in histopathological classification?

reported variation in the proportion of patients with ESRD coded as IDDM or NIDDM needs careful interpretation however, as many NIDDM patients treated with insulin are probably coded as IDDM. Nonetheless, certain differences stand out, e.g. three to four times more IDDM than NIDDM patients with ESRD in Scandinavia; but near equality in Germany, Austria and Southern European Countries [1]. These countries are now accepting over 20 NIDDM patients per million population per year and this figure is projected to double by the year 2000. Overall for Europe, total annual acceptance of diabetic patients for RRT has risen from approximately 2000 in 1983 to over 4000 in 1990 and the proportion coded with NIDDM has risen from approximately 20 % to over 40 % [1].

ESRD in NIDDM: microangiopathy alone?

The histological appearances of diabetic glomerulopathy are identical in IDDM and NIDDM patients with nephropathy. Indeed, most of the early descriptions were in mixed populations of diabetic patients as insulin was the only available treatment [11–13]. More recently, studies at the light and electron microscope level in carefully defined IDDM and NIDDM patients with nephropathy have failed to show any consistent differences [14].

These observations imply a similar pathophysiology in patients with either type of diabetes, but recent data have demonstrated intriguing differences in the function of the microvasculature in IDDM and NIDDM. Jaap and Tooke [15] have shown that capillary pressure and fluid permeability are normal in NIDDM but increased in IDDM patients. They propose that the hyperinsulinaemia that is characteristic of NIDDM may underpin these differences. The

pathophysiological significance of these observations remains to be elucidated however.

A more controversial issue is how often proteinuria in NIDDM patients signifies diabetic or some other glomerulopathy. This topic is discussed at greater length by Steen-Olsen and Mogensen elsewhere in this issue, but in a series of 31 NIDDM patients who were consecutively referred to the St. Bartholomew's Hospital Renal Unit with varying degrees of renal impairment, 29 had a primary diagnosis of diabetic glomerulosclerosis [16]. Table 2 outlines some of the reasons why we feel there is a discrepancy in reported frequency of non-diabetic glomerular pathology in NIDDM patients. Our assessment is that non-diabetic renal disease accounts for less than 10 % of proteinuria in NIDDM patients.

Summary

1. Diabetes (primarily NIDDM) is the commonest single cause worldwide of treated ESRD.
2. Over the past 15 years there has been a 20-fold increase in the acceptance of diabetic patients for RRT in Europe.
3. There are large international variations in the prevalence of IDDM and NIDDM ESRD which may have a genetic/ethnic basis.
4. The wide variation in reported frequency of non-diabetic renal disease in NIDDM patients with proteinuria may be a reflection of referral patterns and probably accounts for less than 10 % of cases.
5. The nature of microangiopathy in NIDDM and any possible differences with IDDM need further study.

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