

Prevalence of nephropathy in the German diabetes population—Is early referral to nephrological care a realistic demand today?

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Abstract

In Germany, diabetes mellitus in the general population has increased to ~8 million people. The implication of this trend for future nephrological care is not well known, as data on this issue are rather limited. Results from different population-based studies suggest that microalbuminuria in diabetic patients is present in 20–30% of the cases. Findings from the diabetes disease management programme in the North-Rhine area revealed the prevalence of chronic kidney disease (CKD) stage II in half of the participants (CKD stage III was present in ~20%). Only a small proportion of this cohort (~1–2%) will reach end-stage renal failure, probably due to the excess mortality risks attributed to advanced kidney disease. Results from the QUASI-Niere registry, which reports on renal replacement therapy in Germany, indicate almost constant incidence and prevalence rates of diabetes in the last 5 years (30.6–34.2% and 23.6–27.1%, respectively). The high percentages of early stages of CKD in the diabetes population indicate a potentially high burden of future nephrological care, especially if patients are referred to nephrologists at an early stage. In reality, in nephrological care, bearing this burden is impossible without expanding the resources for this patient group.

Keywords: chronic kidney disease; diabetes mellitus; health costs; nephrological care; referral politics

Introduction

The recognition of a worldwide pandemic of diabetes mellitus, predominantly type 2 diabetes, is alarming health care officials and the general public. In Germany, about 7 million people are known to have manifested diabetes mellitus, 2 to 3 million are thought to have undetected disease and about 10 million people are diagnosed having impaired glucose tolerance [1]. Between 1988 and 2000, treated cases of diabetes have increased by 43% [2]. Data from regional surveys in Germany suggest that for every detected case with diabetes one case goes undetected [2]. It

is suspected that in the near future every third person in the age group over 65 years will suffer from diabetes mellitus. Despite current efforts to integrate a substantial number of patients into structured disease management programmes (DMPs), a systematic analysis of diabetic patient care in Germany reveals distinctive deficits in transferring recommendations and guidelines into daily patient care [3].

The most important complication of diabetes mellitus is end-stage renal disease (ESRD), accounting for the largest part of the financial burden of diabetes. Although from the patient's view, this complication is one of the most frightening, the high mortality related to the severely increased risk of cardiovascular complications in the stages preceding dialysis is the most important issue in preventive diabetes care. Two cohort studies in both type 1 and type 2 diabetes have found that the likelihood of death from cardiovascular events is about 12 times higher than ESRD [4,5]. Additionally, data from the UKPDS study provide evidence that yearly mortality rates are higher than the rate of progression from one stage of kidney disease to another [6]. Because albuminuria and impaired renal function are both well-established risk factors of cardiovascular morbidity and mortality [7], preventive care in diabetes patients will have to focus on these symptoms. Current guidelines recommend early referral to the nephrologist if serum creatinine exceeds the upper normal limit or hypertension is uncontrolled and antihypertensive therapy has failed to reach the target values [8]. To estimate the burden of nephrological care, data on the early stages of diabetic nephropathy are warranted. As in most other countries, in Germany, these data are not systematically evaluated and published although the routinely collected data of the DMPs would provide an excellent source to measure effects of current intervention. This paper summarizes the outcome of diabetic nephropathy from the available population-based studies of different regions in Germany, and includes findings from a so far unpublished data set of the DMPs in the North-Rhine area.

Definition of nephropathy in diabetic patients

Nephropathy in this context is defined as albuminuria of any degree (in most subjects detected by microalbuminuria screening) and renal insufficiency as calculated by formula

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Table 1. Prevalence of nephropathy in the German diabetes population

	GFR ^a	Population/source	Prevalence
I	>90	General practitioner	30–37% ^b
		Diabetes centers	17.2–19.2% ^c
		Health survey Augsburg	19%
II	60–90		10.4–12.5% ^b
III	30–59	Insurance population	55%
		North-Rhine Participants of DMP-DM 2 (N = 214 579)	19.1–22.7%
IV	15–29		1.0–1.5%
V	<15/dialyse	QUASI-Niere (N = 60 992)	27.9% ^e

^aml/min/1.73 m².^bReference [15].^cReference [13].^dReference [14].^eReference [17].

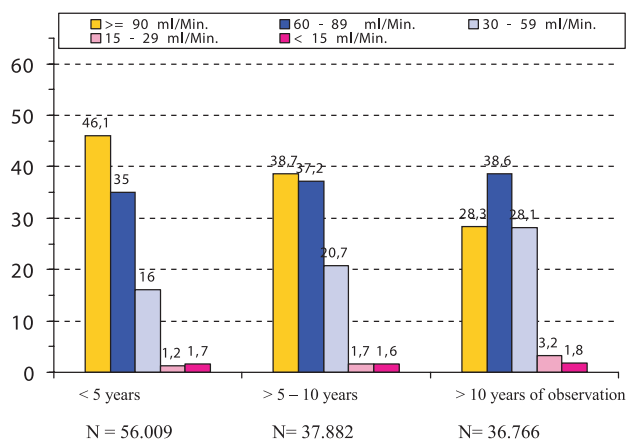
clearances (Cockcroft–Gault or MDRD). Stages of chronic kidney disease (CKD) are classified by renal function (creatinine clearance in ml/min) as defined by current DOQUI guidelines [9]. Therefore, in this context, nephropathy is not necessarily restricted only to diabetic glomerulosclerosis but also to a high proportion of different diseases; frequently, hypertension and macrovascular complications are present [10–12].

Data on stage I–IV nephropathy in diabetic patients

Results on early stages of nephropathy are evaluated in four different study populations. Six hundred diabetic patients recruited from 58 representative outpatient diabetic centres in Bavaria were screened for albuminuria [13]; microalbuminuria was detected in 19.6% in type 1 and 17.2% in type 2; macroalbuminuria was present in 10.8% of the cases (11.7% in type 1 and 7.8% in type 2 diabetes patients). In the KORA study, a random population sample ranging from ages 25 to 74 years showed proteinuria in 19% of the group with type 2 diabetes while 0.7% of the cases underwent dialysis [14]. In a representative study on the prevalence of hypertension and diabetes (HYDRA study), 45 000 patients from 1912 general practitioners were screened [15]. Diabetes was detected in 32% of the men and 28.3% of women. Of these, 37.8% of the patients with diabetes and hypertension tested positive for microalbuminuria. Microalbuminuria was prevalent earlier in only 12.5% of the cases. It can be estimated from these study populations that at least 30% of the diabetes patients in a primary care setting may have CKD stage I (Table 1).

Recent findings from a group of customers of a German insurance company screened for diabetes showed the presence of microalbuminuria in 18% of the cases and a renal clearance <90 ml/min/1.73 m² in 89% of the cases, which is predominantly CKD stages II and III [16].

Currently, about 2 million patients in Germany are included in one of the several diabetes DMPs. Data from more than 50 000 diabetic patients screened in the North-Rhine area were analysed by time under observation and

**Fig. 1.** CKD stages by time of observation (estimated by the Cockcroft–Gault formula); data from diabetes disease management programme in the North-Rhine area.**Table 2.** Incidence and prevalence of diabetes mellitus in the German dialysis population: data from the QUASI-Niere registry (2005)

Diabetes type 1/2	1996	1997	1998	1999	2000	2001	2002	2003	2004
Incidence (%)	30.6	30.7	32.4	33.9	35.7	35.6	35.9	36.2	34.2
Prevalence (%)	21.6	22.3	23.2	24.1	25.0	25.7	26.3	26.8	27.1

stage of CKD (calculated by the Cockcroft–Gault formula) (Altenhofen *et al.* personal communication). The stage of kidney disease increased with time of observation. In the observation period of 5 years, CKD stage II was found in 35% of the cases (>5–10 years, 37%; >10 years, 38%). The proportion of CKD stage III increased gradually with time (<5 years, 16%; 5–10 years, 20%; >10 years, 28%) while that of CKD stages IV and V remained almost unchanged independently from the time of observation (Figure 1). We believe that this finding reflects the high mortality risks of the diabetic population in the advanced stages of renal disease as discussed above.

End-stage renal failure in patients with diabetes mellitus

Best evidence of the development of renal replacement therapy is provided by the German registry QUASI-Niere [17]. At the end of 2004, about 61 000 patients were reported undergoing dialysis therapy; more than 21 000 were alive with functioning grafts. The prevalence and incidence of diabetic patients increased moderately from 21.6% (respectively 30.6%) in 1996 to 27.1% (respectively 34.2%) in 2004 (Table 2). In the last 5 years, the incidence of diabetes in the end-stage renal population remained almost unchanged and exceeded by the increasing trend in vascular nephropathy (Figure 2). In the QUASI-Niere cohort, age-specific mortality of diabetic patients in the age over 75 years is almost identical with the non-diabetic group (Figure 3). This cohort does not include cases that are withheld from dialysis therapy or refused to start dialysis

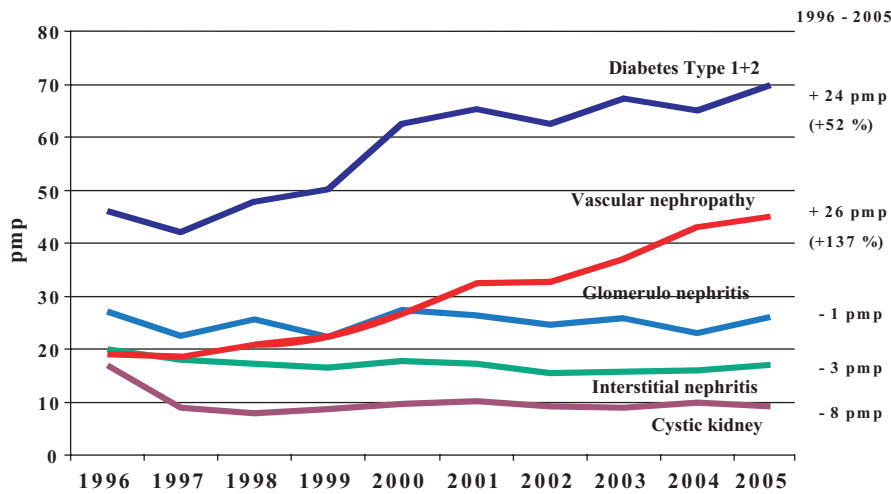


Fig. 2. Incidence trends of different renal diseases in the German dialysis population (data from the QUASI-Niere registry 2007).

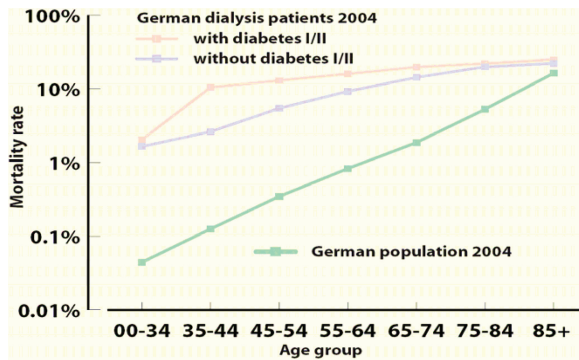


Fig. 3. Age-specific mortality of patients with and without diabetes mellitus undergoing renal replacement therapy (data from the QUASI-Niere registry 2007).

treatment. Furthermore, unreported cases with early mortality within the first months of dialysis are missed.

Are German nephrologists ready to carry the burden of diabetic patients?

Every patient with nephropathy should be screened by a nephrologist. This is completely true in patients with diabetes and nephropathy. While in the early stage of nephropathy distinctive diagnosis of the underlying renal disease has to be established and specific treatment options have to be offered, if available, nephrological care in the advanced stages of CKD must focus on slowing the progression of kidney disease and treating secondary complications. Applying the data on nephropathy in diabetic patients into the reality of medical care, a tremendous workload must be borne by German nephrologists. Arbitrary calculations according to the current guidelines on diabetic care result in 2000–4000 appointments per year for each practising nephrologist (Table 3). Although the contribution of nephrological care in diabetic patients is based on evidence [18], this burden of care is intolerable. With-

Table 3. Estimation of nephrological care in diabetic patients by CKD stages

Stage (GFR) ^a	Suggested need of appointments	Estimated population size	Patients per nephrologist ^b
I–II (60–90)	1 × per year	2–4 million	1850
III (30–59)	2–4 × per year	1.6 million	980
IV (15–29)	Monthly	80–120 000	60
V (<15)	3 × per week	12 000 dialysis patients 4500 ntx patients	10

^aml/min/1.73 m².

^bN = 1634 (data from QUASI-Niere, 2006).

out increasing resources, the demand for early referral of diabetic patients to nephrological care remains a problem. A similar situation was recognized recently in Italy [19].

Summary and perspectives

About 8 million people in Germany suffer from diabetes mellitus. About one-third of them are considered to have some type of kidney disease reflected by albuminuria and decreased renal function. From the estimated number of 1.5 million cases with CKD stage III, a small proportion is progressing to stages IV and V of kidney disease (see Table 1). Only 2000 diabetic patients yearly were accepted for renal replacement therapy. This may reflect the high mortality rates in patients with diabetes and chronic kidney disease. Despite the fact that diabetes mellitus contributes to the biggest proportion of patients starting dialysis therapy, incidence rates of ESRD in this group remained stable in the last 5 years. This is in contrast to the growth of diabetes cases in the general population. The conclusion that the increase in diabetes in the general population leads to a rising tide of diabetic patients on dialysis is not substantiated by the available data.

This observation may reflect both good and bad news: the bad news is that we do not sufficiently care for

mortality risks attributed to nephropathy before reaching ESRD; the good news is that retarding progressive kidney disease extends lifespan before dialysis and keeps patients off from the experience of the sad truth of living a life with dialysis. Besides this, without expanding the number of nephrologists and the resources needed to manage their patients, early care for diabetes patients with nephropathy in Germany remains a wishful thinking so far.

Conflict of interest statement. None declared.

References

- Mehnert H. Diabetes gestern, heute, morgen. *Kompandium Diabetes* 2006; 1: 6–8
- Hauner H. Diabetesepidemie und Dunkelziffer. In: *Deutscher Gesundheitsbericht Diabetes 2006*, Dtsche Diabetes Union, 2005, 7–11
- Martin S, Landgraf R. Systematische analyse der Versorgungssituation bei diabetes mellitus in Deutschland. *Dtsch Med Wochenschr* 2005; 130: 1078–1084
- The DCCT/EDIC Study Research Group. Intensive treatment and cardiovascular disease in patients with type 1 diabetes. *N Engl J Med* 2005; 353: 2643–2653
- Gaede P, Vedel P, Larsen N *et al.* Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N Engl J Med* 2003; 348: 383–393
- Adler AL, Stevens RJ, Manley SE *et al.* Development and progression of nephropathy in type 2 diabetes. The United Kingdom Prospective Diabetes Study (UKPDS 64). *Kidney Int* 2003; 63: 225–232
- Anavekar NS, Pfeffer MA. Cardiovascular risk in chronic kidney disease. *Kidney Int* 2004; 92: S11–S15
- Hasslacher C, Kempe R, Ritz E *et al.* Diabetische Nephropathie (DDG Praxis Leitlinie). *Diabetologie* 2007; 2(Suppl 2): S159–S162
- K/DOQUI. Clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis* 2002; 39(Suppl 1): S1–S246
- Serra A, Romero R, Bayes B *et al.* Is there a need for changes in renal biopsy criteria in proteinuria in type 2 diabetes? *Diabetes Res Clin Pract* 2002; 58: 149–153
- Mazzucco G, Bertani T, Fortunato M *et al.* Different patterns of renal damage in type 2 diabetes mellitus in a multicentric study on 393 biopsies. *Am J Kidney Dis* 2002; 39: 713–720
- Kramer HJ, Nguyen QD, Curhan G *et al.* Renal insufficiency in the absence of albuminuria and retinopathy among adults with type 2 diabetes mellitus. *JAMA* 2003; 289: 3273–3277
- Piehlmeier W, Renner R, Schramm W *et al.* Screening of diabetic patients for microalbuminuria in primary care—the PROSIT-Project. Proteinuria screening and intervention. *Exp Clin Endocrinol Diabetes* 1999; 107: 244–251
- Icks A, Rathmann W, Haastert B *et al.* für die KORA-Studiengruppe. Versorgungsqualität und Ausmass von Komplikationen an einer bevölkerungsbezogenen Stichprobe von Typ 2-diabetespatienten: Der KORA-survey 2000. *Dtsch Med Wochenschr* 2006; 131: 73–78
- Wittchen HU, Krause P, Hofler M *et al.* Aim, design and methods of the “Hypertension and diabetes screening and awareness”—(HYDRA) study. *Fortschr Med Orig* 2003; 121 (Suppl 1): 2–11
- Wolf G, Müller N, Tschauner T, Müller UA. Prävalenz der Niereninsuffizienz im Diabetes TÜV der Deutschen BKK 200–2004. *Med Klin* 2006; 101: 441–447
- Frei U, Schober-Halstenberg HJ. Nierenersatztherapie in Deutschland. Bericht über dialysebehandlung und nierentransplantation in Deutschland 2004/2005, December 2005
- Gandjour A, Lauterbach KW. An evidence-based disease-management program for patients with diabetic nephropathy. *J Nephrol* 2003; 16: 500–510
- Piccoli GB, Grassi G, Mezza E *et al.* Early referral of type 2 diabetic patients: are we ready for the assault? *Nephrol Dial Transplant* 2002; 17: 1241–1247

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