

# Epidemiology of glomerulonephritis in Northern Germany

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## Abstract

**Background** Knowledge of the exact numbers of patients suffering from chronic diseases, possibly requiring costly continuous treatment, is mandatory for future health care plans. Despite some regional biopsy registries, no valid data about the epidemiology of glomerulonephritis in Germany exist, because all publications are hampered by their retrospective character and lack of completeness.

**Methods** In a unique cooperation of out-patient nephrologists with a single major teaching hospital serving a population of approx. 600,000 in the capital of Schwerin and surrounding counties, all patients with abnormal urine findings and/or decreasing renal function of unknown cause were referred for renal biopsy between October 2002 and December 2008. The drop-out rate is assumed to be less than 5%. All biopsies were analysed according to international standards and traditional epidemiological and clinical parameters were collected for comparison with the micro-census of Mecklenburg-Lower Pomerania region of the year 2008. We present the first valid estimations of incidence and 7 year prevalence of glomerulonephritis in Germany.

**Results** In 222 patients, 251 renal biopsies were performed. The annual biopsy rate was 64 per million population (pmp; range 46.2–87.2). The incidence and prevalence of glomerulonephritis over 7 years was 52 and 285 pmp, respectively. The most frequent glomerulonephritis subtype was mesangioproliferative glomerulonephritis (20.9 pmp) followed by focal and segmental glomerulosclerosis (FSGS, 11.2 pmp) of which 43% had an etiologic underlying condition. The incidences of minimal change nephropathy (MCN), membranous nephropathy and necrotising glomerulonephritis (NGN) were 3.2, 5.2 and 4.9 pmp. In one third of all cases, the glomerulonephritis was secondary (incidence of secondary glomerulonephritis 17.5 pmp). Lupus nephritis and ANCA-associated glomerulonephritis were found in 2.9 and 5.4 cases pmp.

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## Introduction

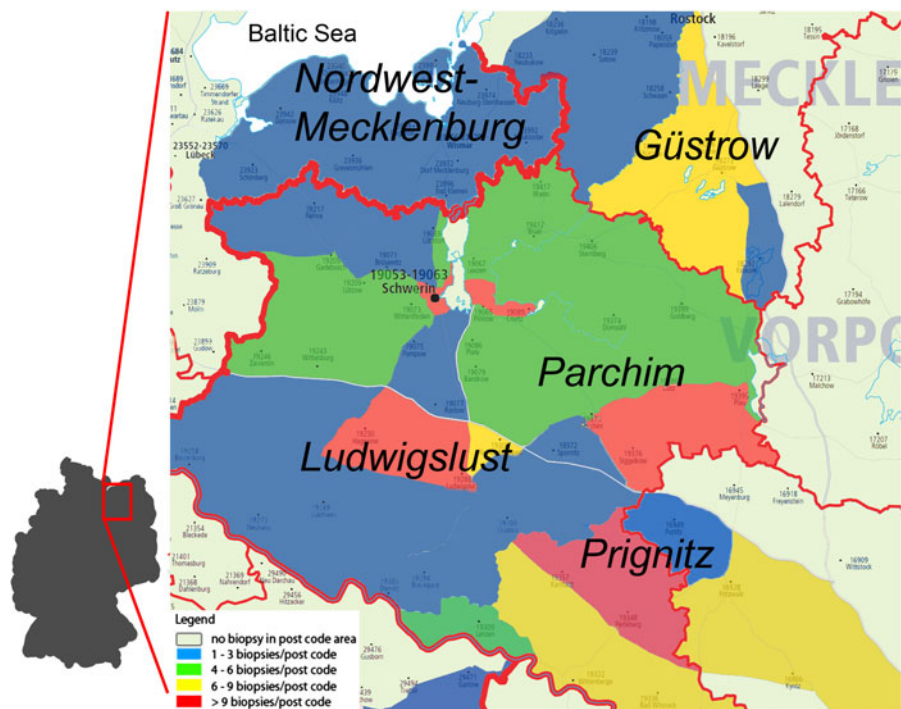
Glomerulonephritis is responsible for 18% of end-stage renal disease cases in people under 65 years-old in the UK [7] and is the cause of ESRD in 16% of all dialysis patients in the US [4]. It is well known that certain entities are more frequent than others and different treatment approaches have been applied with some success. Knowledge about the exact incidence and prevalence of glomerulonephritis and its currently applied regional treatment strategies are mandatory for health care planners to introduce measures for preventing patients from progression to dialysis. However, no valid data about the epidemiology of glomerulonephritis has been reported in Germany so far, because data acquisition is complicated by the decentralized health care structure and the competing dual health-care financing. We report exact data of incidence and prevalence of primary and secondary

glomerulonephritis over a 7 year time interval for a region in Northern Germany.

## Methods

The aim of this study was to improve the detection of glomerulonephritis, its correct diagnosis and the establishment of an early standardized histology-based therapeutic approach. In a unique cooperation of out-patient nephrologists (complete list in appendix) with a single major teaching hospital serving a population of approximately 600,000 in the state capital of Mecklenburg-Lower Pomerania, Schwerin, and surrounding counties (see Fig. 1), patients aged 16 years and older with abnormal urine findings and/or decreasing renal function of unknown cause were referred for renal biopsy between January 2003 and December 2008. In detail, patients with active nephritic urinary sediment and/or proteinuria  $>3.5$  g/day and/or chronic-progressive declining renal function in the absence of diabetes, hypertension or chronic pyelonephritis were eligible for renal biopsy in this study. Renal biopsy was not performed if kidney length was below 10 cm or other signs of severe

**Fig. 1** Patients with renal biopsies between 2003 and 2008 according to post code area (border in red) according to re-drawn from official post code area map by Deutsche Post Direkt GmbH, Bonn 2002



chronic injury were seen on ultrasound. Some of the biopsied patients without urine abnormalities were finally classified as acute renal failure in the presence of congestive heart failure treated with RAAS blockers and diuretics. Renal transplant biopsies and biopsies for acute renal failure were excluded. All patients were primarily seen by their general practitioners and referral nephrologists finally decided on performing the renal biopsy at the tertiary centre. The rate of non-referral was estimated to be less than 5%, as confirmed by telephone survey among referring physicians. Renal biopsies were performed on an over-night admission basis, with previous laboratory and clinical evaluation by either the referring nephrologists or by those in our out-patient department. All biopsies were analysed with light microscopy, immune histology and electron microscopy. All but 11 biopsy readings were performed by the Institute of Cellular and Molecular Pathology at the German Cancer Research Centre, Heidelberg (Prof. Dr. H.J. Gröne). Histological diagnoses were grouped into one of the following 8 categories: minimal change disease (MCN), focal and segmental glomerulosclerosis (FSGS), membranous nephropathy (MGN), membrano-proliferative glomerulonephritis (MPGN), necrotising crescentic glomerulonephritis (NGN), mesangioproliferative glomerulonephritis, including IgA nephropathy (MesGN), secondary glomerulonephritis with immune complex deposition (ICN) and others (including endocapillary glomerulonephritis, anti-glomerular basement membrane disease, and diabetic glomerulosclerosis). All cases were subdivided into primary or secondary glomerulopathies when an underlying condition could be identified (ANCA associated nephritis, lupus nephritis, infection, etc.). When two histopathological patterns were found in one and the same pathology specimen, the therapy-guiding entity was selected; i.e. necrotising glomerulonephritis with IgA nephritis was classified as necrotising glomerulonephritis. The tubulo-interstitial fibrosis was estimated as percentage of the renal cortex and finally categorized into present (>30%) or absent ( $\leq$ 30%).

The following clinical and laboratory parameters were systematically collected at the time of biopsy: gender, age, co-morbidity (ischaemic heart disease, peripheral occlusive artery disease, diabetes), serum creatinine, glomerular filtration rate calculated by the MDRD formula [13], endogeneous creatinine

clearance, 24 h proteinuria, dip-stick proteinuria, systolic and diastolic blood pressure. Hypertension with or without antihypertensive medication at the time of biopsy was defined as systolic blood pressure above 140 mmHg and/or diastolic blood pressure above 90 mmHg. All patients' records were systematically reviewed for outcome and complications between August and November 2009. For patients with FSGS, body weight and height were also extracted from general physicians' medical records.

For epidemiological analysis, the post codes of patients' residences were recorded and the geographical distribution of patients was compared to the micro-census of the state Mecklenburg-Lower Pomerania [10]. All patients were scheduled for trimestrial follow-up visits by either their referring nephrologist or the referral centre.

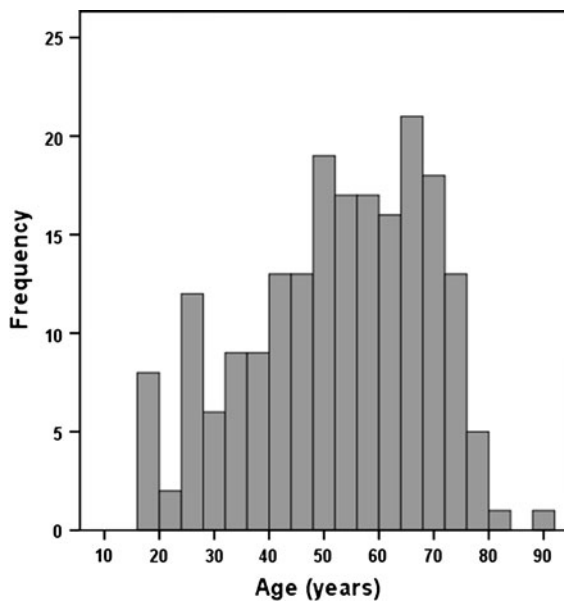
Prevalence was defined as number of patients divided by the population in a specified year multiplied by 1 million (pmp). Incidence was defined as number of newly diagnosed patients divided by the population for a specified year, multiplied by 1 million (pmp). Patients characteristics were given in median and range or mean and standard deviation, as appropriate.

Statistical analysis was performed using PASW Statistics 18 (a courtesy gift by SPSS GmbH Software, München, Germany).

## Results

The total population of the state Mecklenburg-Lower Pomerania was approximately 1.7 million in 2008. The population served by the referral centre (see Fig. 1) declined from 654.268 in the year 2003 to 621.665 (minus 5%) in the year 2008. The male-to-female ratio in the general population was 0.9, and the rate of elderly persons aged 60 years and more was 26.2% in the year 2008 [10]. The number of nephrologists offering renal outpatient services per 100,000 population in the various regions was as following: Schwerin 5.2, Nordwestmecklenburg 1.7, Güstrow 2.7, Ludwigslust 3.2, Parchim 1.0, Prignitz 2.4.

Between 2003 and 2008, 251 renal biopsies were performed in 222 patients, resulting in a biopsy rate of 65.5 biopsies pmp (range 46.2–87.2). All patients were mapped according to their post code area and



**Fig. 2** Age distribution of biopsied patients with glomerular disease

county (see Fig. 1). One hundred and forty patients were male (63%) and mean age was 51 years (range 17–89 years, Fig. 2).

After exclusion of transplant biopsies and renal biopsies for acute renal failure, 130 patients suffered from primary glomerulonephritis, 70 patients were diagnosed with a secondary glomerulopathy and 12 patients had a non-glomerular pathology. Thus, 200 patients (123 males, 77 females) remained for analysis (mean age  $53 \pm 16$  years). The total number of histological subtypes diagnosed as glomerulonephritis are given in Table 1.

### Incidence and prevalence

The mean incidence of glomerulonephritis in the 7-year time period was 52 pmp with a variation from 35 to 67 pmp (see Table 2, last column). According to the follow-up survey in December 2008, 25 patients had died and 34 patients were either on dialysis or end-stage renal disease. The prevalence of biopsy-proven glomerulonephritis was 285 pmp. The most common glomerulonephritis subtype was mesangioproliferative glomerulonephritis MesGN (20.7 pmp) followed by focal and segmental glomerulosclerosis (FSGS, 11.2 pmp), of which 43% had an explaining

**Table 1** Total number of diagnosed histological subtypes subdivided into primary and secondary glomerulopathies

Histological type	Primary	Secondary	Total
MCN	10	2	12
FSGS	24	18	42
MesGN	72	10	82
MPGN	1	2	3
MGN	18	1	19
NGN	1	19	20
ICN	0	7	7
Other	4	11	15
Total	130	70	200

*MCN* minimal change nephropathy, *FSGS* focal and segmental glomerulosclerosis, *MesGN* mesangioproliferative glomerulonephritis including IgA nephropathy, *MGN* membranous glomerulonephritis, *NGN* necrotising glomerulonephritis, *ICN* immune complex nephritis not categorized into one of the classical entities

underlying condition. For IgA nephropathy the 7 years calculated mean incidence in the cohort of biopsied patients was 17.2 pmp. The incidences of minimal change nephropathy (MCN), membranous nephropathy and necrotising glomerulonephritis (NGN) were 3.2, 5.2 and 4.9 pmp, respectively. In one third of all cases, the glomerulonephritis was secondary (incidence 17.5 pmp). Among those, lupus nephritis and ANCA associated glomerulonephritis were found in 2.9 and 5.4 cases pmp. The total number of patients diagnosed with defined glomerulonephritis entities is given in Fig. 3.

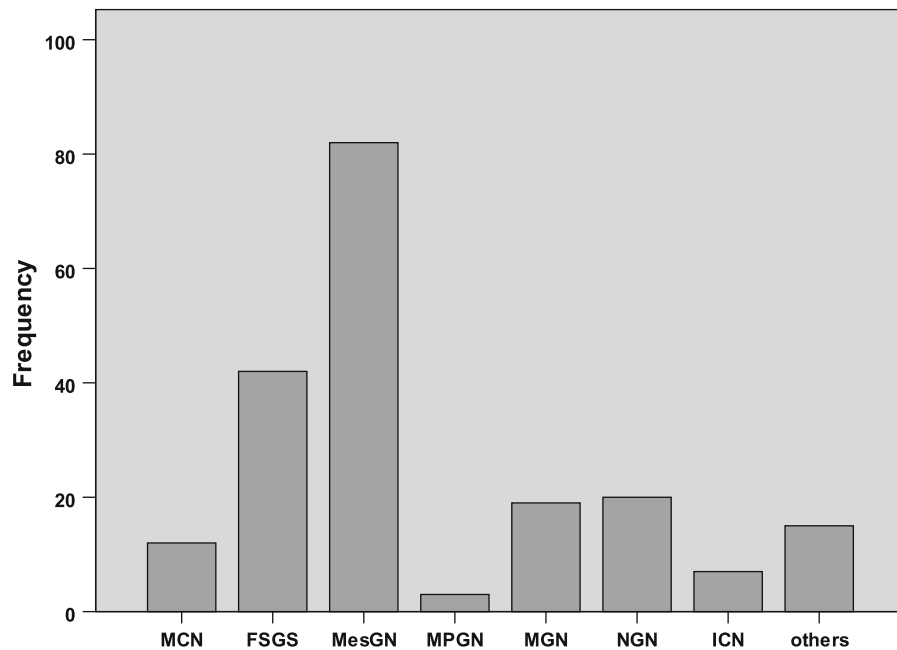
Eight men and 4 women with *minimal change nephropathy* were biopsied. One patient had concomitant diabetes. The median age was 55 years (range 17–73). Median serum creatinine was 90  $\mu\text{mol/l}$  (62–207), median creatinine clearance was 78 ml/min/1.73  $\text{m}^2$  (22–187), and median MDRD-GFR was 36 ml/min/1.73  $\text{m}^2$  (30–42). All were nephrotic with a median proteinuria of 9.5 g/24 h (5.1–27.3). Mean systolic blood pressure was  $135 \pm 14.1$  mmHg and mean diastolic blood pressure was  $79.8 \pm 7.5$  mmHg. Six patients (50%) had blood pressure above 140/90. Almost no tubulointerstitial fibrosis was noted on renal biopsy (mean involvement of renal cortex tissue  $7 \pm 15\%$ ).

*Focal and segmental glomerulosclerosis* was found in 42 patients (27 men, 15 females), median age

**Table 2** Annual incidence for glomerulonephritis in West Mecklenburg-Lower Pomerania

Year	MCN	FSGS	MesGN	MGN	NGN	LN	ANCA	sGN	GN total
2003	1.5	7.6	13.7	3.0	6.1	1.5	4.6	15.3	44.3
2004	1.5	9.2	18.5	6.9	0	1.5	1.5	6.2	38.6
2005	4.7	18.7	26.5	3.1	7.8	3.1	9.3	26.5	66.9
2006	3.1	3.1	18.8	4.7	0	4.7	1.6	11	34.6
2007	1.8	11	27.6	5.5	9.2	1.8	9.2	20.2	62.5
2008	6.4	17.7	19.3	8.0	6.4	4.8	6.4	25.7	62.7
Mean	3.2	11.2	20.7	5.2	4.9	2.9	5.4	17.5	51.6

MCN minimal change disease, FSGS focal and segmental glomerulosclerosis, MesGN mesangioproliferative glomerulonephritis including IgA nephropathy, MGN membranous glomerulonephritis, NGN necrotising glomerulonephritis, LN lupus nephritis, ANCA ANCA associated glomerulonephritis, sGN all secondary glomerulopathies, GN total total incidence of all glomerulopathies for the specified year



**Fig. 3** Frequency of distinct histological entities of glomerular disease over 7 years in Northern Germany. MCN minimal change nephropathy, FSGS focal and segmental glomerulosclerosis, MesGN mesangioproliferative glomerulonephritis,

MPGN membranoproliferative glomerulonephritis, MGN membranous glomerulonephritis, NGN necrotising glomerulonephritis, ICN immune complex nephritis

54 years (17–89). In 18 patients FSGS was associated with diabetes mellitus (6 patients), hypertension (3 patients), end-stage of a necrotising glomerulonephritis (1 patient), FSGS with tubulointerstitial nephritis (1 patient), lupus (1 patient), vasculitis (3 patients), lymphoma (1 patient), sarcoidosis (1 patient), and carcinoma of the prostate (1 patient). The extent of

tubulointerstitial fibrosis in the renal cortex was  $37 \pm 29\%$ . The initial median serum creatinine was  $133 \mu\text{mol/l}$  (50–484), the median creatinine clearance was  $48 \text{ ml/min/1.73 m}^2$  (12–174), and the median MDRD-GFR was  $27 \text{ ml/min/1.73 m}^2$  (11–57). Median proteinuria was  $3.4 \text{ g/24 h}$  (0.3–20.1). Mean systolic and diastolic blood pressure was  $134.5 \pm$

16.8 and  $79 \pm 11$  mmHg. Hypertension was diagnosed in 12 (29%) patients, of which 6 (15%) had blood pressure above 160/95 mmHg. The body mass index in male and female FSGS patients was 29.9 and 28.8 kg/m<sup>2</sup>, respectively.

*Mesangioproliferative glomerulonephritis* was the most frequent diagnosis accounting for 40% of all patients undergoing renal biopsy (male-to-female ratio 2.2:1). IgA nephropathy was found in 66 cases, one patient had IgM nephropathy, three patients showed C3 deposits (one patient showed positive cANCA titres during follow-up) and in 12 patients only mesangioproliferative glomerulonephritis or mesangial hypercellularity without immunoglobuline deposition were reported. In the 10 cases of secondary MesGN the following diagnosis were recorded: sarcoidosis (2 patients), lupus (3 patient), Schönlein-Henoch purpura (3 patients), Schönlein-Henoch purpura with encephalitis disseminata (1 patient), Wegener's granulomatosis (1 patient). Tubulointerstitial fibrosis was reported in 58 biopsies with a mean involvement of  $33 \pm 25\%$  of the renal cortex. Median serum creatinine was 131  $\mu\text{mol/l}$  (56–937), median creatinine clearance was 60 ml/min/1.73 m<sup>2</sup> (6–186), and MDRD-GFR 38 ml/min (5–58). Median proteinuria at presentation was 1.5 g/24 h (0–23.4). Mean systolic and diastolic blood pressure were  $132.8 \pm 14.2$  and  $81.5 \pm 12.1$  mmHg, respectively. Twenty-two (28%) of the patients had hypertension and in 11 patients (14%) blood pressure was above 160/95 mmHg.

In 19 patients *membranous glomerulonephritis* was diagnosed (13 males, 6 females). In one female MGN was associated with systemic lupus erythematosus. Median age was 58 years (30–76). In 13 patients tubulointerstitial fibrosis was measured to involve  $28 \pm 8\%$  of the renal cortex. Renal function measured by median serum creatinine, creatinine clearance and MDRD-GFR were 90  $\mu\text{mol/l}$  (66–213), 90 ml/min/1.73 m<sup>2</sup> (36–162) and 44 ml/min (22–58). Median proteinuria was 6.4 g/24 h (2.4–20.8). Mean systolic and diastolic blood pressure were  $134.8 \pm 17.3$  and  $82.3 \pm 9.9$  mmHg, respectively. Eight patients (42%) had hypertension.

Only three patients were diagnosed with *membranoproliferative glomerulonephritis*. One 75-year-old female presented with cryoglobulinaemia due to hepatitis C. A 58 year old man had idiopathic MPGN type 1 and another 47 year-old patient fulfilled the ARA criteria for systemic lupus erythematosus. All

patients presented with nephrotic syndrome and suffered from hypertension.

#### Necrotising glomerulonephritis with crescents

This heterogenous group of patients was characterized by glomerular crescentic proliferation in at least 50% of glomeruli and rapid deterioration of renal function. Twenty patients were identified. Eight patients had Wegener's disease, 7 patients suffered from microscopic polyangiitis, 3 patients had small vessel vasculitis of skin and kidneys without specific autoantibodies and one patient suffered from NGN and carcinoma of the colon, while the last patient suffered from IgA nephropathy with malignant hypertension. The median age was 69 years (27–78) and male-to-female ratio was 1:1. The percentage of tubulointerstitial fibrosis in the renal cortex was  $45 \pm 28\%$ . The median serum creatinine at the time of biopsy was 345  $\mu\text{mol/l}$  (57–881). The median creatinine clearance was 12 ml/min/1.73 m<sup>2</sup> (6–36). The MDRD-GFR was 16 ml/min (7–42). Proteinuria ranged between 1 and 9.9 g/24 h (median 1.6 g/24 h). Mean systolic and diastolic blood pressure were  $133.5 \pm 18$  and  $76.2 \pm 11.8$  mmHg, respectively. Six patients (32%) had hypertension.

Seven patients suffered from secondary *immune complex nephritis*. Lupus erythematosus was diagnosed in 3 patients, according to the ARA criteria (lupus nephritis type IIa in two patients, lupus nephritis type III in one patient). In the other four patients less than four ARA criteria were diagnosed at the time of biopsy. However, all patients were diagnosed to have lupus nephritis (one patient with thrombotic microangiopathy and type IIa lupus nephritis, one patient with type IIc lupus nephritis and one patient showed a mixture of mesangioproliferative and membranous nephritis while the last patient suffered from classical type IIa lupus nephritis with positive anti-nuclear antibodies and anti-ds DNA antibodies). The male-to-female ratio was 1:3.  $45 \pm 38\%$  of the renal cortex was fibrotic. Median age was 69 years (18–74). Median serum creatinine was 146  $\mu\text{mol/l}$  (63–373), creatinine clearance 60 ml/min/1.73 m<sup>2</sup> (12–156), and MDRD-GFR 34 ml/min (18–47). Median proteinuria was 1.5 g/24 h (0–9.7). Mean systolic and diastolic blood pressure were  $128.6 \pm 24$  and  $75.6 \pm 15.7$  mmHg. Two patients (30%) had hypertension.



### Other histopathologies

Three patients were diagnosed with thin-basement membrane disease, seven patients had amyloidosis of the kidney, and in 3 patients no definite pathology could be detected.

### Comorbidity

Cardiovascular disease was diagnosed at the time of biopsy in 9 (5%) patients, 60 (31%) patients suffered from hypertension, and 37 (19%) patients were diagnosed with diabetes mellitus during follow-up. Thirty seven patients (19%) had more than one comorbidity. Coronary heart disease was seen only in patients with NGN and secondary immune complex nephritis.

### Discussion

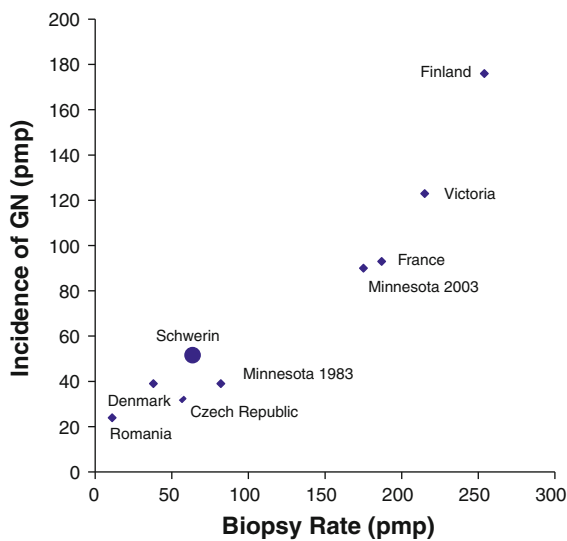
Recent research focuses on the detection of chronic renal disease, because it is associated with high morbidity and mortality, as well as with increasing financial costs of health care [6, 12]. However, publications about the epidemiology of chronic kidney disease do not regularly cover glomerulonephritis as a subgroup because systematic histopathological data are lacking. Systematic data records on glomerular disease in a dual financed health care system as in Germany [11] is even more difficult for various reasons. Firstly, patients are treated by private practitioners as well as by hospital based nephrologists. While the former are mainly involved in the care of dialysis patients, they also usually see patients with urine abnormalities first, but do not establish a histopathological diagnosis by renal biopsy themselves. The latter, although performing invasive diagnostic procedures, have no direct access to patients with mild to moderate renal symptoms and are dependent on the referral policy of private nephrologists. Secondly, nephrologists and hospitals are direct competitors for patients in most regions of Germany making systematic data acquisition difficult. Thirdly, biopsied patients are referred back to nephrologists in private practice, resulting in a loss of follow-up by the centre which performed the biopsy. As a consequence, no reports about the prevalence and annual incidence of glomerulonephritis exist in

Germany and there are only a few publications about the frequency of glomerular disease due to local histopathology registries. This report, however, publishes epidemiological data for Northern Germany on the background of population data. In the region of North-Western Mecklenburg-Lower Pomerania only one referral hospital with co-operating private nephrologists exist and both hospital and nephrology practices serve a well-defined population of more than 600,000.

During the study, the population in that region declined by 5% and annual incidences, as well as 7 year prevalence were calculated on the basis of the existing annual population. The incidence of all glomerulonephritides was 51.6 pmp. Differences in the annual incidence can be the consequence of the small number of patients biopsied per year, reflecting natural variability or may be attributed to changes in referral policies of co-operating nephrologists. Since the publication of Wirta et al. [24], the link between biopsy rate and detection of glomerular pathology in a pre-defined population is well known (see Fig. 4). Even at high biopsy rates, the incidence of glomerulonephritis is probably under-estimated threefold. The mean biopsy rate in the present study (63.5 pmp) is well above other biopsy rates in Europe. However, it is below the large renal biopsy studies in Finland [24], France [19] and Australia [3], indicating that there are still non-detected cases in the Mecklenburg population. Although no direct association between the number of nephrologists and the number of referred patients for renal biopsy could be noted, referrals declined in low-population areas, when less than 3 nephrologists per 100,000 population (Nordwestmecklenburg, Parchim). The highest number of diagnosed glomerulonephritis was found in the close surroundings of nephrology centres (Schwerin, Ludwigslust, cities of Perleberg (county Prignitz) and Parchim (county Parchim)).

One of the strengths of the present paper is its close follow-up, which allows calculation of a population-based prevalence of glomerulonephritis. At least 285 glomerulonephritis patients pmp required nephrological attendance in the year 2008.

It can be noted that the mean age of biopsied patients was 51 years, thus ranging in the top of all biopsy reports. In the state Mecklenburg-Lower Pomerania there is a continuous decline of younger people in favour of the elder generation. The rate of



**Fig. 4** Correlation of biopsy rate and incidence of glomerulonephritis (pmp per million population). The biopsy rate in Schwerin is higher than in Denmark [9], Romania [5] or Czech Republic [18] but significantly lower than in Minnesota [21], France [19], Australia [3] and Finland [24]

persons older than 60 years was 26.2% as compared to Romania (20%, in 2008), Denmark (21%), Czech Republic (21%), Finland (23%), Italy (26%), France (22%) [20]. However, an elder population alone cannot only account for the old age at biopsy, since another recent biopsy report from Germany showed that the mean age of biopsied patients in the region of Northern Rhine West Falia was 52 years [23] despite a younger population with only 25% of persons older than 60 years [14].

The prevalences of identified primary and secondary histological entities is comparable to other reports in Europe and Australia, where MesGN including IgAN is the most commonly diagnosed primary glomerulonephritis and immune-mediated nephritis the most frequent secondary glomerulopathy [3, 8, 9, 18, 24]. However, we report a higher frequency of FSGS (21%), both primary and secondary. This was confirmed by an independent report of the Institute of Pathology at the University of Rostock (Mecklenburg-Lower Pomerania) a few years ago [15], who found that 18% of all biopsied patients suffered from FSGS. The frequency of FSGS in the West German biopsy report was only 13% [23], comparable to the glomerulonephritis epidemiology in Europe. For primary and secondary FSGS, the BMI was found to be 29.9

and 28.8 kg/m<sup>2</sup> in male and females, respectively, indicating an overweight population compared to other regions in Germany and Europe [2]. Obesity might be one factor contributing to the higher prevalence of FSGS in Mecklenburg-Lower Pomerania as it may lead to glomerulomegaly, focal segmental glomerulosclerosis, tubulointerstitial inflammation, and fibrosis [17].

At the time of follow-up after 7 years, 30% of all patients were either dead, on dialysis or uremic. This is comparable to the Danish report, where 32% were dead, 13% terminally uraemic, and 5% uraemic after 10 years [9]. However, only 18% of the Danish patients presented with hypertension in contrast to our cohort with 31% of hypertensive patients at first presentation. Hypertension is a classical predictor of cardiovascular morbidity, and patients with advanced kidney failure regularly develop hypertension. Furthermore, hypertension was a predictor for renal failure in the Danish population. The higher percentage of hypertension at the time of renal biopsy in the Mecklenburg cohort may be due to differences in genetics, ethnic origin, diet or other baseline characteristics. Manifest hypertension was most frequent in FSGS and MesGN patients, while patients with other glomerulopathies showed modest blood pressure elevation between 140/90 and 160/95 mmHg. Nevertheless, the mean blood pressure of all patients with or without antihypertensives described in this study was comparable to healthy persons in a cohort study of chronic kidney disease with cardiovascular co-morbidity from Reykjavik [6], supporting the hypothesis that glomerulonephritis patients (at least in the early stages) are different from patients with other chronic kidney diseases and probably have a lower risk of cardiovascular morbidity in the initial phase of the disease.

Beside the older age in the Mecklenburg patients, special attention should be paid to the high incidence of tubulo-interstitial fibrosis (28% in MGN, 33% in MesGN and 37% in FSGS). Tubulo-interstitial fibrosis is often associated with long-standing glomerular disease and is associated with declining renal function [1, 22] and hypertension [16]. Under this aspect, it can be postulated that patients may have been referred rather late for histopathological diagnosis.

In summary, the 52 pmp incidence of glomerulonephritis in North-East Germany is reliable but strongly dependent on the biopsy rate and referral policy of cooperating private nephrologists. The high



rates of hypertension and tubulo-interstitial fibrosis may indicate late referral for biopsy while the unusual high frequency of FSGS in the North-East could reflect metabolic and obesity associated factors in the development of this disease. Since dialysis-dependent end-stage renal failure is a major burden for both, the involved patient and the financing health care system, major efforts should be undertaken to increase the biopsy rate at an earlier state of the disease followed by specific and symptomatic treatment in order to slow down or prevent terminal renal failure.

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**Conflict of interest** There is no conflict of interest.

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