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The Italian experience of the national registry of renal biopsies

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The Italian experience of the national registry of renal biopsies.

Background. Although several registries collecting data of patients with kidney diseases exist, there are only a few registries which specifically collect data relating to renal biopsy; one such registry is the Italian Registry of Renal Biopsies (IRRB). The aim of this study was to report on the relative frequency of nephropathies according to gender, age at time of biopsy, clinical presentation and renal function, based on the histologic diagnosis during the years 1996 to 2000.

Methods. We evaluated data relating to 14607 renal biopsies, provided by 128 renal units in Italy. Data entry was performed by using the Internet-based database directly (URL *http://www.irrb.net*). Clinical presentation was defined as urinary abnormalities (UA), nephrotic syndrome (NS), acute nephritic syndrome (ANS). Renal diseases were divided in four major categories: (*1*) primary glomerulonephritides (GN); (*2*) secondary GN; (*3*) tubulointerstitial nephropathies (TIN); and (*4*) vascular nephropathies (VN).

Results. Primary GN, TIN, and VN were more frequent in males compared to females while secondary GN was more frequent in females. Diseases whose frequency was higher in males were IgA nephropathy (IgAN), benign nephroangiosclerosis (BNA), and acute tubular necrosis (ATN). A significantly higher frequency of immune-mediated secondary GN, as well as primary GN, including minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS), and mesangiocapillary GN (MCGN), was shown in females. Primary and secondary GN, TIN, and VN were more frequent in the range 15 to 65 years of age. At the time of biopsy 77% of primary GN and 61% of secondary GN presented with normal renal function. Acute renal failure (ACR) was more present in TIN (52%), while chronic renal failure (CRF) was more frequent in VN (47%).

Conclusion. We believe collection of data relating to renal biopsies in a national registry is a useful tool for nephrologists in that it meets one of the current challenges facing the clinical research enterprise. The availability of these data will allow epidemiologic studies in health care to answer the several open questions in both prevention and treatment of renal diseases.

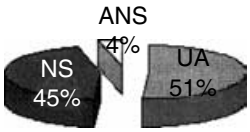
One of the key features for the development of good quality clinical epidemiologic research has been identified in the development of adequate flexible databases for the collection of epidemiologic data relating to specific diseases [1]. Although several registries collecting data of patients with kidney diseases exist [2–7], there are only a few registries which specifically collect data relating to renal biopsy; one such registry is the Italian Registry of Renal Biopsies (IRRB) [8–11]. In 1987, the Renal Immunopathology Study Group of the Italian Society of Nephrology started this registry. During the years 1987 and 1988 data of renal biopsies were collected by specific questionnaires filled out by the participating centers. Only limited information was collected, mainly data of the histologic diagnosis. Since 1989 and up to 1995, additional information were collected, including age, gender, clinical presentation, and renal function at the time of renal biopsy [8–11]. In 1996, a more complete version of the paperwork was generated and translated into a user-friendly relational database. Information collected in the database included a variety of indicators, such as serum creatinine, daily proteinuria, blood pressure, height and body weight, viral markers, clinical presentation, hemoglobin values, and current medications [12]. At present, all the information collected in the database is also accessible via the Internet. This system allows sharing of materials among the involved participating centres. Data available in the IRRB are being used for epidemiologic studies both at a local and national level.

The aim of this study was to report on the relative frequency of nephropathies according to gender, age, clinical presentation and renal function, based on the histologic diagnosis.

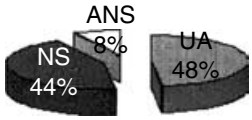
METHODS

We evaluated data relating to 14,607 renal biopsies collected in the IRRB during the years 1996 to 2000. These data were provided by 128 renal units in Italy. Data entry was performed by using the Internet-based database directly (URL *http://www.irrb.net*). Each participating center was assigned a user ID and password to access the site for consultation and data entry. We considered gender, age at time of biopsy, clinical presentation [defined

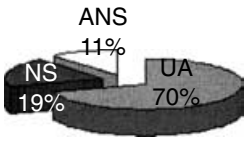
Key words: renal biopsy, registry, nephropathies.



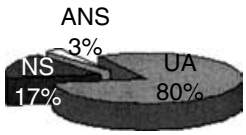
Primary GN	NS %	ANS %	UA %	P (chi-square)
IgAN	6.8	32.6	59.7	P < 0.0001
MGN	44.1	3.8	6.3	P < 0.0001
FSGS	16.9	3.8	10.6	P < 0.0001
Non-IgAN	5.3	9.6	12.3	P < 0.0001
MCD	16.7	1.0	3.1	P < 0.0001
MPGN	8.1	11.3	4.9	P < 0.0001
Crescentic GN	1.4	21.6	1.6	P < 0.0001
Acute post-Str. GN	0.7	16.2	1.4	P < 0.0001
Total (100%)	3178	291	3521	



Secondary GN	NS %	ANS %	UA %	P (chi-square)
Immune-mediated GN	45.2	80.9	63.7	P < 0.0001
MEDAGN	22.5	2.2	28.4	P < 0.0001
DAGN	30.4	0.0	5.1	P < 0.0001
IDAGN	1.4	16.9	1.9	P < 0.0001
LDAGN	0.1	0.0	0.4	P = 0.3500
MAGN	0.3	0.0	0.4	P = 0.7215
Total (100%)	1039	178	1131	



Tubulointerstitial Nephropathy	NS %	ANS %	UA %	P (chi-square)
CTIN	31.8	25	62.7	P < 0.0001
ATIN	18.2	58.3	20.9	P = 0.0002
ATN	13.6	12.5	5.7	P = 0.1562
MM-associated TIN	36.4	4.2	10.8	P < 0.0001
Total (100%)	44	24	158	



Vascular Nephropathy	NS %	ANS %	UA %	P (chi-square)
BNA	73.6	37.5	86.6	P = 0.0002
TM	20.8	50.0	5.9	P < 0.0001
MNA	3.8	12.5	5.5	P = 0.5857
CN	0.0	0.0	0.4	P = 0.8861
EPH	1.9	0.0	1.6	P = 0.9236
Total (100%)	53	8	253	

Fig. 1. Frequency of histologic diagnosis on the basis of clinical presentation of nephropathy. Abbreviations are: IgAN, IgA nephropathy; MGN, membranous GN; FSGS, focal segmental glomerulosclerosis; non IgAN, mesangioproliferative GN without IgA deposits; MCD, minimal change disease; MCGN, mesangiocapillary GN; MEDAGN, metabolic and hereditary disorder–associated GN; DAGN, dysgammaglobulinemia-associated GN; IDAGN, infectious disease–associated GN; LDAGN, liver disease–associated GN; MAGN, malignancy-associated GN; CTIN, chronic tubulointerstitial nephropathy; ATIN, acute tubulointerstitial nephropathy; ATN, acute tubular necrosis; MM-associated TIN, multiple myeloma-associated tubulointerstitial nephropathy; BNA, benign nephroangiosclerosis; TM, thrombotic microangiopathy; MNA, malignant nephroangiosclerosis; CN, cortical necrosis; EPH, preeclampsia; NS, nephrotic syndrome; ANS, acute nephritic syndrome; UA, urinary abnormality.

as urinary abnormalities (UA), nephrotic syndrome (NS), acute nephritic syndrome (ANS)], and renal function.

Renal diseases were divided in four major categories: (*1*) primary glomerulonephritides (GN); (*2*) secondary GN; (*3*) tubulointerstitial nephropathies (TIN); and (*4*) vascular nephropathies (VN).

Mesangial glomerulonephritis (both IgA and non IgA mesangial nephropathy), membranous GN (MGN), focal segmental glomerulosclerosis (FSGS), minimal change disease (MCD), mesangiocapillary GN (MCGN), crescentic GN and poststreptococcal GN were considered as primary GN. Immune-mediated GN (systemic lupus erythematosus, Schönlein-Henoch purpura, amyloidosis, Goodpasture's syndrome, necrotizing vasculitis, connective disease, and sarcoidosis), metabolic and hereditary-disorder-associated GN (MEDAGN) (diabetes mellitus, Alport's syndrome, Fabry disease, nail-patella syndrome, congenital NS, and other hereditary disorders), dysgammaglobulinemia-associated GN (DAGN) (essential mixed cryoglobulinemia, Waldenstrom's macroglobulinemia, monoclonal gammopathy, and light-chain disease), infectious disease–associated GN (IDAGN) (nonstreptococcal GN, endocarditis, ventriculoatrial shunt nephritis, and others), liver disease–associated GN (LDAGN), and malignancy-associated GN (MAGN) were considered as secondary GN. Chronic TIN (CTIN), acute TIN (ATIN), acute tubular necrosis (ATN), and multiple myeloma-associated TIN were considered among TIN. Benign nephroangiosclerosis (BNA), thrombotic microangiopathy (TM), malignant nephroangiosclerosis (MNA), cortical necrosis (CN), and preeclampsia (EPH) were considered among VN.

Data of 905 renal biopsies which could not be adequately classified due to inadequate data entry or

Table 1. Italian Immunopathology Group, SIN

City	Hospital	Chief	Referring
Aosta	Regionale	Alloatti	Gaiter
Torino	G. Bosco	Quarello	Rollino-Beltrame
Torino	Molinette	Piccoli	Stratta
Torino	CMID	Roccatello	Alpa
Torino	Reg. Margherita	Coppo	Porcellini
Alessandria	Ospitalieri	Iberti	Demicheli
Biella	Degli Infermi	Bajardi	Caramello
Novara	Della Carità	Verzetti	Chiarinotti
Borgomanero	SS. Trinità	Cavagnino	Airoldi
Cuneo	S. Croce	Ghezzi	Canepari
Ivrea	Civile	Giacchino	Aimino
Milano	S. Raffaele	Bianchi	Slaviero
Milano	Maggiore	Ponticelli	Banfi
Milano	Niguarda	Civati	Confalonieri
Milano	S. C. Borromeo	Colasanti	Ferrario
Milano	Sacco	Barbiano	Genderini
Milano	S. Paolo	Brancaccio	Volpi
Milano	Fatebenefratelli	Sorgato	Castiglione
Milano	De Marchi	Edefonti	Giani
Lodi	Maggiore	Imbasciati	Farina
Melegnano	Predabissi	Grassi	Lupi
Cin. Balsamo	Bassini	Buccianti	Saruggia
Legnano	Civile	Guastoni	Levati
Magenta	G. Fornaroli	Novi	Baroli
Monza	S. Gerardo	Redaelli	Malnati
Vimercate	Osp. di Vimercate	Sessa	Righetti
Treviglio	Consorziale	Borghi	Moriggi
Brescia	P.O. di Montichiari	Brandi	Bassi
Brescia	Spedali Civili	Maiorca	Strada
Como	S. Anna	Grillo	Grillo
Lecco	A. Manzoni	Locatelli	Pozzi
Busto Arsizio	Civile	Giangrande	D'Amato
Cremona	Ist. Ospitalieri	Malberti	Bufano
Sondrio	Civile	Pedrini	De Cristofaro
Mantova	Carlo Poma	Tarchini	Baraldi
Pavia	Clinica del Lavoro	Salvadeo	Segagni
Pavia	Pol. S. Matteo	Dal Canton	Esposito
Genova	DIMI	Deferrari	Garibotto
Genova	S. Martino	Cannella	Mulas
Genova	Gaslini	Perfumo	Barbano
Imperia	Civile	Cavatorta	Re
Trento	S. Chiara	Rovati	Comotti
Udine	S. Maria Misericordia	Mioni	Boscutti
Udine	Università	Romano	
Trieste	Osp. Di Cattinara	Panzetta	Savoldi
Trieste	Garofalo	Pennesi	
Dolo	Civile	Meneghel	
Chioggia	Civile	Munaretto	Urso
Feltre	Civile	Nachtigal	Antonucci
Pordenone	S. Maria degli Angeli	Tesio	Raimondi
Treviso	Civile	Calconi	Dugo
Castelfranco Veneto	S. Giacomo	Cascone	De Fino
Padova	Univ. Pediatria	Zacchello	Murer
Camposampiero	P. Cosma	Bonadonna	
Verona	Civile Maggiore	Maschio	Lupo
Bologna	Malpighi	Zucchelli	Pasquali
Bologna	S. Orsola	Stefoni	Frascà
Rimini	Degli Infermi	Cagnoli	Rigotti
Parma	Riuniti-Nefrologia	Cambi	Allegri
Ravenna	S. Maria delle Croci	Fusaroli	Fabbri
Reggio Emilia	S. Maria Nuova	Borgatti	Rustichelli
Ferrara	S. Anna	Gilli	Stabellini
Modena	Policlinico	Albertazzi	Furci
Firenze	Careggi	Salvadori	Bergesio
Firenze	Meyer	Bartolozzi	Lavoratti
Prato	Civile	Amato	Aterini
Bagno a Ripoli	S. Maria Annunziata	Maggiore	Nigrelli
Arezzo	S. Maria	Sasdelli	Bizzarri
Pisa	Dip. Di Med. Interna	Bianchi	Panichi
Pisa	S. Chiara	Rindi	Pasquariello-Basini
Ancona	Umberto I	Mioli	Fanciulli
Roma	Pol. Umberto I	Cinotti	Pecci
Roma	Fatebenefratelli	Chiappini	Selvaggi
Roma	Tor Vergata	Splendiani	Costanzi
Roma	S. Giovanni	Balducci	Gamberini
Roma	S. Camillo Forlanini	Di Giulio	De Paolis
Roma	Lazzaro Spallanzani	Cherubini	
Roma	Sant'Eugenio	Casciani	Meloni
Roma	Sandro Pertini	Paone	Galliani
Roma	Bambin Gesù	Rizzoni	
Ostia	G.B Grassi	Friggi	Fortunato
Viterbo	Degli Infermi	Ancarani	Feriozzi
Formia	P.O. Formia	Moscoloni	Treglia
Perugia	Silvestrini	Buoncristiani	Brugnano
Pescara	Santo Spirito	Ciofani	D'Andrea
Chieti	Pol. San Camillo	Bonomini	Amoroso
Napoli	University Federico II	Andreucci	Balletta
Napoli	II Università-Nefrologia	De Santo	Pollastro
Napoli	Pellegrini	Sorice	Nuzzi
Napoli	Santobono	Pecoraro	Pota-Fella
Avellino	S. Giuseppe Moscati	De Simone	Iannaccone
Salerno	S. Giovanni di Dio	Cioffi	Ricci
Polla	L. Curio	Pagano	Gigliotti
Bari	Policlinico	Schena	Manno
Bari	Santa Rita	La Raia	
Bari	Policlinico- Pediatria	Penza	Aceto-Francioso
Bari	Giovanni XXIII	Caringella	Messina-Puteo
Acquaviva	Miulli	Chiarulli	Cazzato-Casucci
Altamura	Civile	Petrarulo	Pallotta
Monopoli	San Giacomo	Pastore	Grasso
Putignano	Santa Maria degli Angeli	Giannattasio	Gernone
Foggia	Ospedali Riuniti	Procaccini	
S. G. Rotondo	Sollievo Sofferenza	Stallone	D'Errico
San Severo	Teresa Maselli	Avanzi	Casale
Taranto	SS. Annunziata	Di Maggio	
Manduria	M. Giannuzzi	Chimienti	Distratis
Martina Franca	Osp. Gioia	Basile	Montanaro
Lecce	Vito Fazzi	Mastrangelo	Patruno
Scorrano	I. Veris delli Ponti	Tasco	Stefanelli
Galatina	Santa Caterina Novella	Gigante	Gallucci
Matera	Osp. Riuniti	Lopez	Santarsia
Reggio Calabria	Melacrino	Zoccali	Martorano
Cosenza	Annunziata	Bonofiglio	De Napoli
Catanzaro	Policlinico-Nefrologia	Fuiano	Marino
Palermo	Civico	Visconti	
Palermo	Catt. Di Med Interna	Cerasola	Li Vecchi
Palermo	G. Cristina	Maringhini	Sapia
Palermo	Sez. Tecn. Emodialitica	Galione	
Catania	Vittorio Emanuele	Spata	Spanti
Catania	Università	Fatuzzo	Rapisarda
Catania	San Luigi	Liuzzo	Figura
Catania	Cannizzaro	Di Landro	Seminara
Messina	Catt. Medicina Int.	Buemi	Pettinato
Messina	Regina Margherita	Giorgianni	Gattarello
Messina	Policlinico-Nefrologia	Bellinghieri	Santoro
Siracusa	Umberto I	Daidone	Pagano
Cagliari	Brotzu	Altieri	Pani
Sassari	Ist. Patologia Medica	Satta	Cigni

biopsies which were nondiagnostic (inadequate sampling of materials, normal renal tissue) or diagnoses of end-stage kidney diseases, were not included in the present analysis.

Data are reported as prevalence and were coded in contingency tables and compared by χ^2 test.

RESULTS

We considered 14,607 renal biopsies, of which 89.9% were from native and 10.1% were from transplant kidneys. Of all diseases of native kidney, primary GN were the most frequent (64.3%), followed by secondary GN (24.7%), TIN (5.3%) and VN (4.7%).

Primary GN were more frequent in males (64%) compared to females (36%); similarly true for TIN (males 57% and females 43%) and VN (males 70% and females 30%). On the contrary, secondary GN were more frequent in females (males 45% and females 55%). Diseases whose frequency was higher in males were IgA nepropathy (IgAN) (males 39.3% and females 27.8%; $P < 0.0001$), BNA (males 75.8% and females 56.1%; $P < 0.0001$), and ATN (males 18.8% and females 11.1%, $P < 0.01$). A significantly higher frequency of immune-mediated secondary GN (males 55.9% and females 72.5%; $P < 0.0001$) as well as primary GN, including MCD (males 7.4% and females 10.3%; $P < 0.0001$), FSGS (males 12.3% and females 14.7%; $P < 0.005$), and MCGN (males 6.2% and females 8.0%; $P < 0.005$) was shown in females.

In terms of age at the time of renal biopsy, primary and secondary GN, TIN, and VN were most frequent in the range 15 to 65 years of age. Below the age of 15 the most frequent primary GN was MCD (<15 years 23.3%, 15 to 65 years 7.3%, and >65 years 7.5%; $P < 0.0001$), and the most frequent secondary GN were MEDAGN (<15 years 30.4%, 15 to 65 years 20.0%, and >65 years 16.3%; $P < 0.0001$). The most frequent TIN were CTIN (<15 years 60.6%, 15 to 65 years 48.2%, and >65 years 30.0%; $P < 0.0001$), and the most frequent VN was TM (<15 years 63.6%, 15 to 65 years 17.4%, and >65 years 13.8%; $P < 0.0001$). On the contrary, above the age of 65 the most frequently biopsied nephropathies for VN were BNA (<15 years 18.2%, 15 to 65 years 67.4%, and >65 years 80.7%; $P < 0.0001$), the most frequent among primary and secondary GN was MGN (<15 years 3.5%, 15 to 65 years 18.0%, and >65 years 45.2%; $P < 0.0001$), and the most frequent among TIN was MM-associated TIN (<15 years 0.0%, 15 to 65 years 9.8%, and >65 years 25.8%; $P < 0.0001$).

Figure 1 indicates the clinical presentation of histologically ascertained nephropathies. The main reasons for performing a renal biopsy were UA (51% of cases of primary GN, 48% of cases of secondary GN, 70% of cases of TIN, and 80% of cases of VN). The type of nephropathies which most frequently presented with NS were MGN (44.1%), FSGS (16.9%), and MCD (16.7%) among primary GN, MM-associated TIN (36.4%) among TIN, and DAGN (30.4%) among secondary GN. The diseases which most frequently presented with ANS among primary GN were crescentic GN (21.6%), MCGN (11.3%), and poststreptococcal GN (16.2%). Among secondary GN the ones most frequently presenting with ANS were immune-mediated GN (80.9%) and IDAGN (16.9%); among TIN, these were ATIN (58.3%), and among VN these were TM (50.0%). Nephropathies which were most frequently associated with UA were BNA (86.6%) among NV, CTIN (62.7%) among TIN, and IgAN (59.7%) among primary GN.

Finally, at the time of biopsy 77% of primary GN and 61% of secondary GN presented with normal renal function. Acute renal failure was mainly present in TIN (52%) while chronic renal failure was mainly present in VN (47%).

DISCUSSION

We confirm previously published data that renal diseases are more frequent in men, with the exception of secondary GN [10, 11, 14]. The higher relative frequency of secondary GN in females may be explained by the immune-mediated nature of these forms of GNs associated with systemic lupus erythematosus which occurs more frequently in this gender. We found that all categories of renal diseases occur mainly between the ages of 15 and 65; this may well be explained by the tendency not to perform biopsies in elderly patients and the practice of performing renal biopsies in children only when the disease is persistent in time and presenting with major relevant symptoms. In our data, FSGS and MCD, which typically affect children, were not very represented compared to MGN, which, as is known, is typical of adult age. Finally, the diagnosis of primary and secondary GN is generally done in the absence of renal function abnormalities; this indicates the current tendency of both doctors and patients not to undervalue syndromes associated with renal diseases and urinary abnormalities in particular.

CONCLUSION

We believe collection of data relating to renal biopsies in a national registry is a useful tool for nephrologists in that it meets one of the current challenges facing the clinical research enterprise [1]. The availability of these data will allow epidemiologic studies in health care to

answer the several open questions in both prevention and treatment of renal diseases.

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