Analysis of biopsy-proven nephrotic syndrome in Tibetan patients

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To the Editor: Nephrotic syndrome (NS) is a common clinical syndrome characterized by massive proteinuria and hypoalbuminemia, but it has never been investigated in the Tibetan population. This was a single-center, retrospective study of Tibetan patients who underwent renal biopsy from 2009 to 2016 in West China Hospital of Sichuan University. All patients aged over 14 years were included. Exclusion criteria were insufficient pathological material, transplant kidney biopsies, and pregnancy. Renal pathological characteristics were defined according to the World Health Organization standards and histological glomerular disease classification protocols. Quantitative and qualitative data are expressed as mean ± standard deviation and percentages, respectively. Student's *t* tests or Mann-Whitney tests were used to compare parametric or nonparametric continuous variables, respectively. χ^2 and Fisher exact tests were used to compare qualitative variables. All statistics were analyzed by SPSS 23.0 software (SPSS Inc., Chicago, IL, USA); $P < 0.05$ was considered statistically significant.

We included 122 Tibetan NS patients with a mean age of 36.8 ± 13.6 years (57.4% male). The urinary protein and serum albumin levels were 8.9 ± 8.5 g/24 h (range 3.5–53.3 g/24 h) and 21.2 ± 5.2 g/L, respectively. The serum creatinine level was 91.6 ± 60.7 μmol/L. Hypertension (32.8%) and diabetes mellitus (7.4%) were prevalent comorbidities [Supplementary Table 1, http://links.lww.com/CM9/A737]. The most common histopathological diagnosis was membranous nephropathy (MN; $n = 42$ [34.4%]), followed by minimal change disease (MCD; $n = 18$ [14.8%]), and immunoglobulin A nephropathy (IgAN; $n = 15$ [12.3%]); diabetic nephropathy (DN) and lupus nephritis (LN) each accounted for 7.4% (both $n = 9$) [Table 1]. Less common causes included focal segmental glomerulosclerosis and membranoproliferative glomerulonephritis ($n = 5$ [4.1%] each); hepatitis B virus-associated glomerulonephritis ($n = 4$ [3.3%]); and Henoch–Schonelein purpura glomerulonephritis, mesangial proliferative glomerulonephritis, and sclerosing glomerulonephritis ($n = 3$ [2.5%] each). The histopathologic spectrum showed sex differences [Table 1]. The frequencies of MCD (21.2% *vs.* 10%) and LN (11.5% *vs.* 4.3%) were higher in females, while that of DN (1.9% *vs.* 11.4%) was lower. The spectra of NS in different age groups were significantly different ($P = 0.041$). Among patients aged 14 to 24 years, MN and MCD were the most common causes of NS (25.8%). The most common diagnosis was MN in the 25 to 44 (41.5%), 45 to 59 (31.0%), and ≥60 (33.3%) years of age groups. The second most common causes in these age groups were LN (13.2%), DN (20.7%), and IgAN (22.2%), respectively [Table 1].

A cross-sectional study showed that 19.1% of Tibetan adults have at least one indicator of kidney damage, which is higher than in other parts of China.[1] Zhou *et al*[2] reported that the most common kidney disease in the Tibet Plateau was primary glomerulonephritis, mainly manifesting as NS, but the study did not exclude Han subjects. It was not surprising that MN (34.3%) and MCD (14.8%) were the two dominant pathological types. This was similar to another large-scale study conducted in China and investigations in Spain and Italy.[3] However, it was different from Hong Kong (China), Denmark, Korea, and Japan, where the most common cause of NS was MCD followed by MN.[4] Mostly ethnic Han patients were included in the Beijing and Hong Kong studies. The dominance of MN could be explained by the fact that its frequency in China has risen over the past decade. However, LN and DN, each accounting for 7.4%, were the most common secondary causes of NS in this study. The percentage of DN was much higher than results from Beijing (0.72%). It is uncommon for patients with an established DN diagnosis to undergo kidney biopsy, so the proportion of renal biopsy-proven DN was relatively low in China. However, our patients did not provide accurate diabetic history or had short-term diabetes. All nine diabetic patients with NS were diagnosed with DN by pathology examination, indicating poor disease management in the Tibetan population, although Tibetan individuals had a significantly lower prevalence of diabetes

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Table 1: Histopathological spectrum of patients with nephrotic syndrome between different genders and ages.

Variables	Total ($n=122$)	Male ($n=70$)	Female ($n=52$)	Average age (years)	14 to 24 years ($n=31$)	25 to 44 years ($n=53$)	45 to 59 years ($n=29$)	≥60 years ($n=9$)
MN	42 (34.3)	23 (32.9)	19 (36.5)	37.3 ± 12.3	8 (25.8)	22 (41.5)	9 (31.0)	3 (33.3)
MCD	18 (14.8)	7 (10.0)	11 (21.2)	34.3 ± 15.2	8 (25.8)	4 (7.5)	5 (17.2)	1 (11.1)
IgAN	15 (12.3)	10 (14.3)	5 (9.6)	35.8 ± 16.2	5 (16.1)	5 (9.4)	3 (10.3)	2 (22.2)
DN	9 (7.4)	8 (11.4)	1 (1.9)	48.8 ± 9.3	0	2 (3.8)	6 (20.7)	1 (11.1)
LN	9 (7.4)	3 (4.3)	6 (11.5)	35.1 ± 8.1	1 (3.2)	7 (13.2)	1 (3.4)	0
FSGS	5 (4.1)	3 (4.3)	2 (3.8)	28.4 ± 7.8	1 (3.2)	4 (7.5)	0	0
MPGN	5 (4.1)	4 (5.7)	1 (1.9)	34.4 ± 11.9	1 (3.2)	3 (5.7)	1 (3.4)	0
HBVGN	4 (3.3)	3 (4.3)	1 (1.9)	37.75 ± 15.6	1 (3.2)	2 (3.8)	1 (3.4)	0
HSPGN	3 (2.5)	1 (1.4)	2 (3.8)	19.7 ± 3.2	3 (9.7)	0	0	0
MsPGN	3 (2.5)	1 (1.4)	2 (3.8)	44.3 ± 17.0	1 (3.2)	1 (1.9)	0	1 (11.1)
Sclerosing glomerulonephritis	3 (2.5)	3 (4.3)	0	40.0 ± 13.5	0	1 (1.8)	2 (6.9)	0
Others	6 (4.9)	4 (5.7)	2 (3.8)	–	2 (6.5)	2 (3.8)	1 (3.4)	1 (11.1)

Data were shown as mean ± standard deviation, or *n* (%). –: Not applicable. DN: Diabetic nephropathy; FSGS: Focal segmental glomerulosclerosis; HBVGN: Hepatitis B virus-associated glomerulonephritis; HSPGN: Henoch–Schonelein purpura glomerulonephritis; IgAN: IgA nephropathy; LN: Lupus nephritis; MCD: Minimal change disease; MN: Membranous nephropathy; MPGN: Membranoproliferative glomerulonephritis; MsPGN: Mesangial proliferative glomerulonephritis.

than Han participants. Notably, renal amyloidosis, one of the most common causes of nephrotic-range proteinuria in the elderly, was not found among Tibetan patients, possibly due to the small sample size. The average ages of male and female patients were similar and do not explain the observed sex differences. Although some studies found that metabolic syndrome was significantly lower for Tibetan males, glucose intolerance was not sex associated in people living at high altitudes. Factors involved in endothelial dysfunction have been found among preclinical Tibetan young males, which may explain the different disease spectra between males and females. Diagnosis varied with age. Unexpectedly, MN was also the most common cause of NS in patients 14 to 24 years old, with most in stage I. Since few patients had anti-phospholipase A2 antibody test results, secondary MN could not be eliminated.

The study was limited by several weaknesses. First, the small number of patients may affect the generalizability of our results to the Tibetan population. Second, the restrictions of geographic distance and socioeconomic status led to selection bias for undergoing renal biopsy. In conclusion, this study investigated NS in the Tibetan population. MN and MCD were the main causes of NS in the Tibetan population. The histopathologic spectrum varied in genders and different age group.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consents for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

None.

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