

Disease burden of IgA Nephropathy in China

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Introduction

- IgA nephropathy is a primary glomerulonephritis (PGN) characterized by the deposition of the IgA antibody in the glomerulus. About one-third PGN patients have been diagnosed with IgA nephropathy worldwide, and the proportion is higher in Asia. [1]
- The clinical presentation of IgA nephropathy is heterogeneous, from simple hematuria to acute glomerulonephritis and renal failure. Without effective treatments, IgA nephropathy could progress to end-stage renal disease (ESRD).[2]
- The pathogenesis of IgA nephropathy remains elusive and specific treatment of IgA nephropathy are unclear.

Objective

To conduct a systematic literature review on epidemiology, burden of disease, quality of life and clinical treatment of IgA nephropathy in China.

Methods

Literature Retrieval

- Chinese electronic databases: Weipu Periodical Resource Integration Service Platform (VIP), Chinese National Knowledge Infrastructure database (CNKI), Wanfang Data Knowledge Service Platform (WANFANG)
- English electronic databases: PubMed, Embase
- Date of publication: 2010.01.01 ~ 2020.12.10

Inclusion Criteria

- The study included adult patients with IgA nephropathy.
- The study population was Chinese or mainly Chinese. (Mainland China only)
- The literature included at least one outcome indicator on epidemiology, burden of disease, quality of life, and clinical treatment.
- Literature on the burden of disease and quality of life for chronic kidney disease (CKD) and end stage renal disease (ESRD) was also searched.
- Literatures are full texts published in Chinese or English.

Exclusion Criteria

- Duplicate publications
- Epidemiological survey of local population with sample size < 200

Results

Literature Review

- A total of 4,609 publications were retrieved (4,000 in Chinese and 609 in English). After duplicate removal, a total of 2,789 publications were screened, and 59 publications were included for detailed review.
 - 19 publications on epidemiology; 6 on economic burden; 7 on quality of life; and 27 on clinical treatment

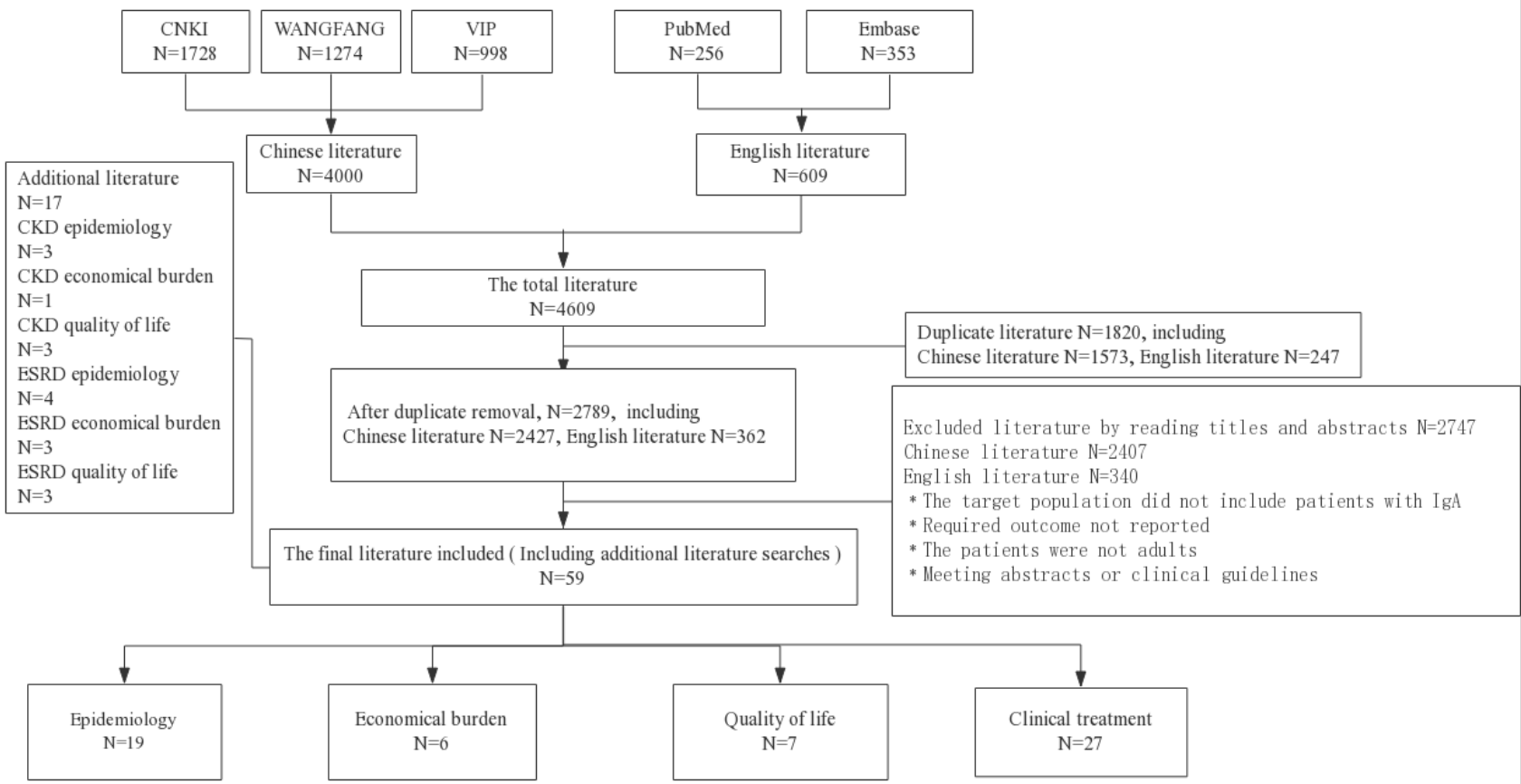


Figure 1: Literature Retrieval Process

Epidemiology

- IgA nephropathy is more prevalent among young adults, The mean age of IgA nephropathy patients at first diagnosis was **30.5~40.0 years old**, and patients aged 25~44 years accounted for 57.1%~67.0 of all patients[3-5]. **There was no significant gender difference.** [4,5]
- PGN is the most frequently diagnosed glomerular disease varying from 65.1% to 78.8% (weighted mean 70.5%) in all renal needle biopsies; IgA nephropathy is the most common PGN, accounting for 34.0% to 52.7% (weighted mean 37.8%). Therefore, **the diagnosis rate of IgA nephropathy in patients with renal biopsy was about 24.1%~41.0%** (weighted mean was 26.7%).[3-7] The epidemiological studies of IgA nephropathy in China are shown in Table 1.
- Based on the study on the epidemiology and composition of disease spectrum of CKD, GN and PGN in China, we selected nationally representative studies and epidemiological summary data to estimate the number of adult patients with IgA nephropathy in China, **which is about 4.59 million, of which about 570,000 have been diagnosed** [3-8] as illustrated in Figure 2.

Economic Burden

- The average hospitalization cost of patients with IgA nephropathy was about **4,867~14,900 yuan** [9-11]
- The hospitalization costs mainly include the cost of renal biopsy, medications, laboratory tests (blood pressure, blood albumin, blood creatinine, eGFR, 24h urine protein quantitative, C-reactive protein); **the drug cost accounted for 26.6%~59.1%** of the total hospitalization cost. [9-11]
- The outpatient follow-up rate within 6 months after discharge was about 81%. [10]
- For those patients who have progressed to ESRD, the annual per capita direct treatment costs for peritoneal dialysis and hemodialysis was were 73,000 - 96,000 yuan and 87,000 - 120,000 yuan, respectively. The medical costs were also positively associated in the presence of co-morbidities, including anemia, hypertension, diabetes and dyslipidemia.[12-15]
- From 2015 to 2016, the number of ESRD patients receiving dialysis in China was about 578,000~608,000. When patients received peritoneal dialysis and hemodialysis, the total direct medical expenditure was estimated to be around 50.7 billion to 51.9 billion yuan. Of the expenses associated with dialysis, 76.0% was covered by medical insurance. Therefore, medical insurance needs to pay 38.6 billion to 39.4 billion yuan for dialysis patients every year. **Although ESRD patients account for only 0.2% of the total insured population, Medicare payments account for 2.4% of Medicare funds.** [12,16]
- If ESRD continues to progress after dialysis, the patient may need a kidney transplant. The annual per capita direct medical expenses are higher, about 195,000-203,000 yuan in the first year, including the expenses of immunosuppressant drugs and hospitalization incurred by the donor and recipient during the operation period. In the second and third year, the cost was reduced somewhat, but it still reached 67,000 to 104,000 yuan [14,17]

Table 1: Epidemiological study of IgA nephropathy in China

References	Enrollment time	Renal biopsy	PGN	PGN detection rate	IgA	IgA detection rate	Proportion (IgA/PGN)
[3]	2003~2014	36,379	26,386	72.5%	9,746	26.8%	36.9%
[4]	2001~2015	176,355	126,031	74.0%	42,584	24.1%	34.0%
[5]	1993~2010	40,759	27,349	67.1%	14,583	35.8%	52.7%
[6]	/	10,779	8,494	78.8%	4,418	41.0%	50.0%
[7]	2009~2018	34,630	22,529	65.1%	8,343	24.1%	37.0%
Total	/	298,902	210,789	70.5%	79,674	26.7%	37.8%

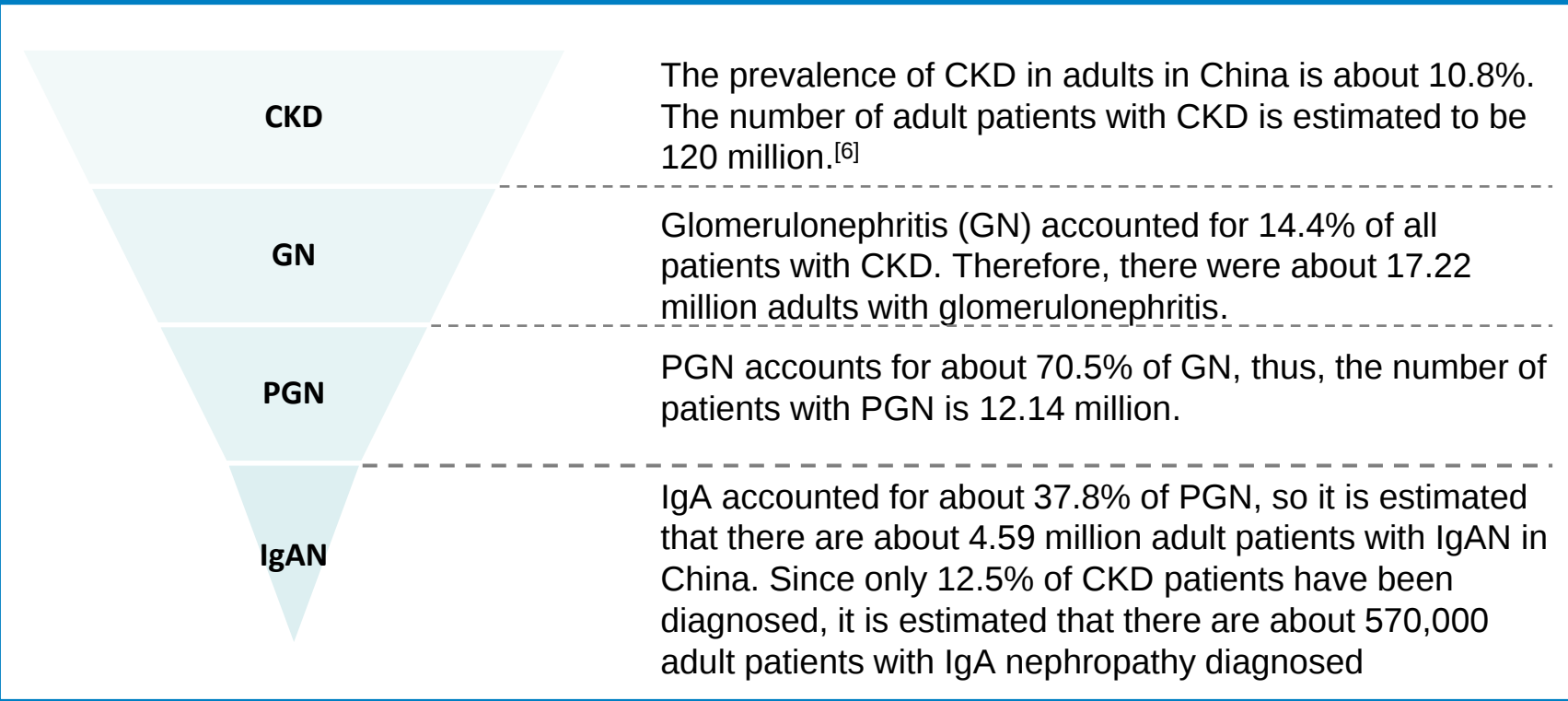


Figure 2: Number of adult patients with IgA nephropathy in China

Quality of Life

- The study using the SF-36 to evaluate the quality of life of patients with IgA nephropathy showed that **poor mobility and lower SF-36 PCS score. (39.9~41.6)**[18]
- About **30% of patients with IgA nephropathy develop depressive symptoms**. Using the Beck Depression Inventory II(BDI-II) scale, 70% of the patients had moderate to severe depressive symptoms, which affected their SF-36 MCS score and quality of life. [18]
- Patients with IgA nephropathy who progress to ESRD have poor mobility and quality of life due to disease symptoms, malnutrition, anemia, insomnia, and loss of muscle mass due to long-term dialysis treatment**
- Age, education level, marital status, comorbidities, complications, and duration of dialysis all affect patients' quality of life. [19-21]
- With the increase of dialysis time, the risk of death gradually increased. Retrospective study on the survival prognosis of ESRD in China shows that **the annual mortality rate of ESRD patients undergoing hemodialysis in China is about 3.8%~11.2%, which is higher than that of the general population (50 ~ 64 years old was 0.4% ~ 1.0%)**, and the primary cause of death is cardiovascular and cerebrovascular events and systemic failure. [22-23]

Clinical Treatment

- The rate of receiving RAAS inhibitors in patients with IgA nephropathy ranged **from 90.0% to 96.2%** [22,24-27], Losartan potassium or valsartan was used more frequently, accounting for more than 85% [28]
- The treatment rate with glucocorticoids (oral methylprednisolone or prednisone) was about **10.8%~53.7%** [24,25, 22,26,29-30].
- About **2.4%~33.2% of patients were treated with immunosuppressant** [22,24-26,29], including Mortimecofenate (MMF), cyclophosphamide (CYC), cyclosporine (CsA), tacrolimus (TAC) and leflunomide (LEF).[22,24,26,30-31]
- Many patients were also treated with traditional Chinese medicine, which is mainly based on Tripterygium wilfordii polyglycosides, and the treatment rate is about 72%. [22]
- For compliance, the utilization rate of RAAS inhibitors for 6 months and above was 89.0%-90.0%. [22,26-27,32-33]; The initial dose of glucocorticoids was 0.4~1.0mg/kg/d, and the dose was typically reduced after 2 months, and the drug was discontinued after 6 to 12 months of use[28,30,32,34-37]
- For efficacy, **60.4%~74.4% of patients with IgA nephropathy can achieve remission after 6 months of treatment** [26,29]. Urine protein remission was achieved in 37.3% of patients using RAAS inhibitors alone (TA-P<1g) [26]. In patients with poor control after treatment with RAAS inhibitors, the combination of RAAS inhibitors with glucocorticoids or immunosuppressants significantly reduced short-term urinary protein levels and delayed renal function progression. (Reduce the rate of EGFR decline) [28,36-41]. **However, the long-term benefit of RAAS inhibitors in combination with glucocorticoids or immunosuppressants in patients with IgA nephropathy remains unclear.**
- For safety, few studies have reported adverse events of RAAS inhibitors, an RCT reported one case of neutropenia and one case of hyperkalemia after RAAS treatment [39]. The main adverse events of glucocorticoids and immunosuppressive agents were diabetes, infection (mainly upper respiratory tract and lung infection), insomnia, abnormal liver function and Cushing's syndrome. [39,42]

Conclusion

In China, IgA nephropathy is the most common PGN, with a large number of patients. And because there are currently no medications specifically approved for this condition, as the disease progresses to ESRD, IgA nephropathy takes significant toll on patients' quality of life and carries heavy economic burden to both patients and society.

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