Proceedings of Anticancer Research, 2023, Volume 7, Issue 2
http://ojs.bbwpublisher.com/index.php/PAR
ISSN Online: 2208-3553
ISSN Print: 2208-3545

Risk Factors of Infection in Nephrotic Syndrome

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Abstract: *Objective:* To determine the risk factors of infection in patients with nephrotic syndrome. *Methods:* A retrospective study was conducted on 155 patients with nephrotic syndrome under our department from January 2019 to December 2019. Among them, 43 cases had infection, and the rate of infection was 27.74%. The risk factors of infection were analyzed. *Results:* Among the 155 patients with nephrotic syndrome, 43 cases developed infection, including 3 cases of upper respiratory tract infection (6.98%), 33 cases of lower respiratory tract infection (76.74%), 3 cases of skin infection (6.97%), 3 cases of urinary tract infection (6.97%), and 1 case of facial nerve infection (2.32%). Compared with the group without infection, the group with infection had lower serum albumin and immunoglobulin G (IgG) levels as well as higher serum creatinine and 24-hour urinary protein levels ($P < 0.05$). Multivariate logistic regression analysis showed that decreased serum albumin (odds ratio [OR] = 1.14; $P < 0.01$) and IgG (OR = 1.1; $P < 0.144$) were independent risk factors for infection. *Conclusion:* Respiratory infection is the most common infection in nephrotic syndrome, and the decrease in serum albumin and IgG are independent risk factors for infection.

Keywords: Nephrotic syndrome; Infection; Risk factors

Online publication: March 30, 2023

1. Introduction

Nephrotic syndrome is characterized by proteinuria, hypoproteinemia, edema, and hyperlipidemia. Infection is one of the most common complications of nephrotic syndrome, which affects the prognosis of such patients, easily leads to recurrence, and increases the hospitalization and mortality rates of such patients [1]. In this study, 155 patients with nephrotic syndrome from January 2019 to December 2019 were retrospectively analyzed, among which 43 patients developed infection as a complication. Risk factors related to these patients were analyzed to develop a better understanding of the susceptibility of patients with nephrotic syndrome to infection, improve the prevention of infection, reduce the occurrence of infection, improve the remission rate of kidney disease, and reduce the financial burden on patients.

2. Patients and methods

A retrospective study was conducted on 155 patients with primary nephrotic syndrome under our department from January 2019 to December 2019. The diagnostic criteria of nephrotic syndrome were as follows: massive proteinuria > 3.5 g and hypoproteinemia < 30 g/L, which may be accompanied by edema and hypertension.

The general data of the patients (sex, age, course of immunosuppressant treatment, and hormone dose) and laboratory test results (white blood cell count, platelet count, neutrophil count, lymphocyte count, urine protein quantification, serum albumin, serum creatinine, C-reactive protein [CRP], immunoglobulin G [IgG], *etc.*) were collected.

The patients were classified into different groups: without infection, with infection, existing infection on admission, infection after treatment (hormone or immunosuppressant), and intensive care unit (ICU) admission. The patients were further categorized according to the site of infection: upper respiratory tract infection, lower respiratory tract infection, urinary tract infection, skin and soft tissue infection, *etc*.

SPSS 22.0 was used for statistical analysis. If the measurement data were in accordance with normal distribution and homogeneity of variance, they were expressed as mean ± standard deviation, and the comparison between groups was analyzed by Student-Newman-Keuls (SNK) test. If the measurement data did not obey the normal distribution and/or meet the homogeneity of variance, they were expressed as median (25%–75% quantile), and Kruskal-Wallis H test was used for comparison between groups. The indicators with statistically significant differences in univariate analysis were included in logistic regression for multivariate analysis to explore the risk factors for infection in patients with nephrotic syndrome. $P < 0.05$ was considered statistically significant.

3. Results

A total of 155 patients with nephrotic syndrome were retrospectively analyzed, among which 43 developed infection, and the rate of infection was 27.74%, as shown in **Table 1**.

Table 1. Incidence of infection in patients with nephrotic syndrome

Total number of cases	Infected cases	Proportion (%)
155	43	27.74

Among the 43 patients with infection, 3 cases had upper respiratory tract infection, 33 cases had lower respiratory tract infection, 3 cases had skin infection, 3 cases had urinary tract infection, and 1 patient had facial nerve infection. See **Table 2** for more details.

Table 2. Distribution of infection sites

Site of infection	Number of cases (n, %)
Upper respiratory tract	3 (6.98)
Lower respiratory tract	33 (76.74)
Skin infection	3 (6.97)
Urinary tract infection	3 (6.97)
Facial nerve infection	1 (2.32)

Among the 43 cases, 18 had infection on admission, accounting for 41.86%, 21 cases developed infection after receiving hormone or immunosuppressant, accounting for 48.83%, 3 cases were admitted to the ICU, accounting for 6.97%, and 1 case died, accounting for 2.32%. See **Table 3** for more details.

Table 3. Distribution of infection timing

Timing of infection	Number of cases (n, %)
Existing infection on admission	18 (41.86)
Infection after treatment	21 (48.83)
Admission to the ICU	3 (6.97)
Number of deaths	1 (2.32)

We also found significant differences in serum albumin, 24-hour urinary protein, IgG, and serum creatinine among the groups ($P < 0.05$); the aforementioned indicators were all lower in the group with infection than in the group without infection ($P < 0.05$). However, there was no significant difference among the group with existing infection on admission, the group with infection after treatment, and the group admitted to the ICU. **Table 4** shows the comparison of data.

Table 4. Comparison of the clinical data of each group

Groups / Indicators	Without infection	Existing infection on admission	Infection after treatment	Admitted to the ICU	With infection	P	P1	P2	P3
Age	52.09 ± 13.15	52.72 ± 18.92	53.70 ± 12.81	63.00 ± 4.74	53.23 ± 16.53	0.678	0.665	0.837	0.247
White cells ($\times10^9$/L)	6.92 (5.31–8.27)	7.49 (4.63–8.00)	7.59 (6.66–9.84)	12.57 (10.11–13.2)	7.64 (5.67–8.53)	0.007	0.024	0.242	0.063
Neutrophils ($\times10^9$/L)	3.82 (3.07–5.96)	4.17 (2.65–6.01)	5.03 (3.91–6.52)	10.45 (8.40–11.05)	5.01 (3.81–6.44)	< 0.001	0.002	0.365	0.036
Lymphocytes ($\times10^9$/L)	1.89 (1.30–2.75)	1.53 (1.23–2.77)	1.66 (1.24–2.09)	1.02 (0.85–1.52)	1.57 (1.13–2.05)	0.069	0.029	0.279	0.67
Platelets ($\times10^{12}$/L)	251.84 ± 74.09	253.66 ± 95.58	262.85 ± 69.82	318.75 ± 140.26	265.39 ± 91.11	0.524	0.364	0.733	0.219
Serum albumin (g/L)	20.00 ± 0.00	20.00 ± 5.69	27.00 ± 0.00	19.75 ± 4.32	20.55 ± 4.98	0.003	0.002	0.591	0.641
Urine protein (g/dL)	6.39 (4.40–8.00)	7.34 (6.11–9.85)	7.51 (5.54–9.00)	7.45 (6.25–9.51)	7.45 (5.69–9.65)	0.048	0.016	0.629	0.938
Serum creatinine (μmol/L)	68 (58.25–77.55)	74 (61.5–78)	82.5 (64–112)	113.5 (94.25–141.75)	77.0 (63–100)	0.002	0.01	0.095	0.163
IgG (g/L)	6.16 (4.67–7.95)	4.75 (2.66–6.88)	4.41 (2.50–5.97)	5.91 (4.79–7.14)	5.03 (2.64–6.85)	0.034	0.019	0.579	0.296

Abbreviations: ICU, intensive care unit; IgG, immunoglobulin G; P1, comparing between the group without group and the group with infection; P2, comparing between the group with existing infection on admission and the group with infection after treatment; P3, comparing between the group with infection after treatment and the group admitted to the ICU; P, comparing among groups.

The multivariate logistic regression analysis of infection-related factors showed that serum albumin (odds ratio [OR] = 1.14; $P < 0.01$) and IgG (OR = 1.1; $P < 0.144$) were independent risk factors for infection (**Table 5**).

Table 5. Multivariate logistic regression analysis of infection-related factors in the group with infection

Variable	B (K)	SE (B)	χ^2	*P*-value	OR	95% CI
Serum albumin	0.134	0.041	1	0.001	1.14	1.238
Urine protein (g/dL)	-0.11	0.047	1	< 0.001	0.9	0.817–0.981
Serum creatinine (μmol/L)	0.026	0.008	1	0.001	0.98	0.96–0.99

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Variable	B (K)	SE (B)	χ^2	*P*-value	OR	95% CI
IgG (g/L)	0.099	0.068	1	0.144	1.1	0.967–1.261

Abbreviations: CI, confidence index; B, unstandardized beta; IgG, immunoglobulin G; K, number of predictor terms; OR, odds ratio; SE, standard error.

4. Discussion

Infection is one of the most common complications in nephrotic syndrome [2-6]. Infection is the leading cause of all-cause mortality in primary nephrotic syndrome. Through multicenter cohort studies, Yamamoto [7] revealed that infection is the leading cause of death in patients with nephrotic syndrome and is more common in patients with minimal change disease than in those with membranous nephropathy, suggesting that patients with minimal change disease are susceptible to infection. Xu [8,9] showed the incidence of complications in nephrotic syndrome, attributing 27.14% to infection, 3.68% to thromboembolism, 9.38% to acute renal insufficiency, and 67.17% to lipid metabolism disorder. Infection is a common complication in nephrotic syndrome, and the common infection sites are the respiratory tract, urinary tract, and skin. Gulati [11] showed that children with complications of infection in nephrotic syndrome have significantly lower serum albumin levels compared with those without infection and suggested that hypoproteinemia is an independent risk factor for infection in patients with nephrotic syndrome. Singh *et al*. [12] found that low IgG level is a risk factor for nephrotic syndrome complicated with severe infection. Our analysis showed that the group with infection, compared with the group without infection, had lower serum albumin and IgG levels and higher serum creatinine and urine protein levels; the differences between the groups were statistically significant. Multivariate logistic regression analysis showed that serum albumin and IgG are independent risk factors for infection. This finding is consistent with previous research results. We suggest that hypoalbuminemia and serum IgG levels are important risk factors of infection in patients with nephrotic syndrome.

The impairment of immune function by glucocorticoids increases the incidence of opportunistic infections [19-21], which are also considered a significant cause of mortality in patients. With long-term use of glucocorticoids, the body's humoral and cell-mediated immune response are affected to varying degrees, and the decrease of IgG levels in humoral immunity is an independent risk factor of infection in patients with nephrotic syndrome [22-24]. In terms of cell-mediated immunity, glucocorticoids may cause $CD4^+$ T cells apoptosis, which increases the susceptibility to infection [25,26].

Both Chen *et al*. and Grijalva *et al*. established that the risk of infection in various autoimmune diseases is positively correlated with the dose of glucocorticoids used [27,28]. The study showed that among all the patients with infection, the proportion of patients using glucocorticoids was about 72.09%, and the serum IgG level in the infected patients was significantly lower. The logistic regression analysis showed that low IgG level is an independent risk factor for infection.

In conclusion, infection is one of the common complications in nephrotic syndrome, with the respiratory system being the most common targeted site. Our analysis showed that the serum albumin and IgG levels of patients with infection were lower than those of patients without infection, while the serum creatinine and urine protein were higher in the former group compared to the latter. This suggests that serum albumin and IgG are independent risk factors for infection. In the diagnosis and treatment of patients with nephrotic syndrome, the factors predisposing to infection should be considered before the use of glucocorticoids or immunosuppressants to prevent the occurrence of infection, which may affect the prognosis of patients and even lead to the death of patients.

Disclosure statement

The authors declare no conflict of interest.

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