ORIGINAL ARTICLE

Clinical Features of Nephrotic Syndrome in Children

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ABSTRACT We reviewed 129 new patients with primary nephrotic syndrome (PNS) admitted to the Department of Child Health Sardjito Hospital from January 1986 to December 1995. Most patients were males, i.e., 96 or 74.4%, giving a male to female ratio of 2,9:1. The number of patients under the age of 6 years was 66 (or 51.2%), slightly greater than the number of patients over the age of 6 years (63 patients, or 48.8%). Nephritic symptoms consisting of hematuria, hypertension and azotemia were more frequently found in patients over the age of 6 years, and in non-responder patients. With prednisone treatment, 108 (0r 83.7%) of patients were steroid responders, and 21 (or 16.3%) were non-steroid responder. **[Paediatr Indones 1997; 37: 13-19]**

Introduction

Nephrotic syndrome can occur at any moment, during the course of a primary or secondary glomerular disease. Therefore, nephrotic syndrome is not an independent disease, but constitutes a functional condition which is related to glomerular dis ease.[1-3] The incidence of nephrotic syndrome in children is reported to be 2 per 100,000 children under the age of 10 years.[4] The syndrome is more frequently found in males than in females, with a ratio of about 2:1, and the greatest proportion is in children aged 2-3 years. Even though it is not a hereditary disease, there is a familial tendency for the disease in 2-8% of patients.[2] Nephrotic syndrome is recognizable by the occurrence of various clinical symptoms consisting of massive proteinuria (50

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mg/kg BW/24 hours, or 40 mg/m²/hours, or 1 gram/m²/24 hours), hypoalbumin emia (<2.5 gram/dl), hypercholesterolemia (>250 mg/dl) and edema,[5-7] occasionally accompanied by hematuria, hypertension, or decreased kidney function.[5,7] Of all primary nephrotic syndrome patients, 80% are of minimal changes.[8] Corticosteroids and cyclophosphamide drugs are used in the treatment of nephrotic syndrome with the presumption that nephrotic syndrome is an immunopathological disease.[5,8] Although treatment with corticosteroid and cytotoxic drugs is sufficiently successful, to date it is not as yet definitely known how the immunological process actually works.

There are various methods and dosages for administrating the corticosteroid medication, but an effort towards uniformity or standardization of corticosteroid administration has been made by the Internatonal study of Kidney Disease in Children (ISKDC) in 1967.[9] This paper reports on the clinical course and response of the treatment of children with nephrotic syndrome treated in our Department.

Methods

This study was conducted during 10 years, from January 1986 to December 1995, on new nephrotic syndrome patients admitted to the Department of Child Health, Medical School, Gadjah Mada University - Sardjito Hospital, Yogyakarta, Indonesia. The diagnostic criteria for the primary nephrotic syndrome are the occurrence of edema, massive proteinuria (1 gram/m²/24 hours), hypoalbuminemia (<2.5 g/dl) and hypercholesterolemia (>250 mg/dl).

Other systemic diseases causing secondary nephrotic syndrome, i.e. systemic lupus erythematosus, Henoch Schonlein purpura, amyloidosis, diabetes mellitus, malaria, metabolic diseases, and others were not included in this study. In the assessment of the results of laboratory examination, the following standardization was applied: hematuria was defined as red blood cells > 5 per one eye field from centrifuged urine; normal blood urea (20-40 mg/dl), normal serum creatinine (0.6-1.2 mg/dl), whereas hypertension was defined as diastolic blood pressure > 95 mmHg, as recommended by the "Task Force of Blood Pressure in Children, 1977).[10]

The method and dosage of steroid medication, which in this case was prednisone, was in accordance with the recommendation of the 1967 "International Study of Kidney Disease in Children (ISKDC)",[9] i. e., prednisone at 60 mg/m²/day or 2 mg/kgBW/day for 4 weeks, subsequently continued with a dosage of 40 mg/m²/day given intermittently 3 days each week during the following 4 weeks. A patient was classified as responder if the patient showed remission results during 8 week treatment, whereas those who did not show remission during this time period were called as steroid resistant patients. Remission criteria were disappearance of edema and a negative proteinuria for 3 consecutive days in 1 week. Immunosuppresive drug, i.e. cyclophosphamide at 2 mg/kgBW/day was administered to steroid resistant patients.

Results

During the 10-year period from 1986 to 1995, 129 new patients who fulfilled the study criteria were treated. The number of male patients was 96 (74.4%), and female patients 33 (25.6%), giving a male to female ratio of 2.9:1. The patients aged between 8 months and 14 years, with an average age of 6.9 years. The distribution of patients according to age and sex is shown in Figure 1.

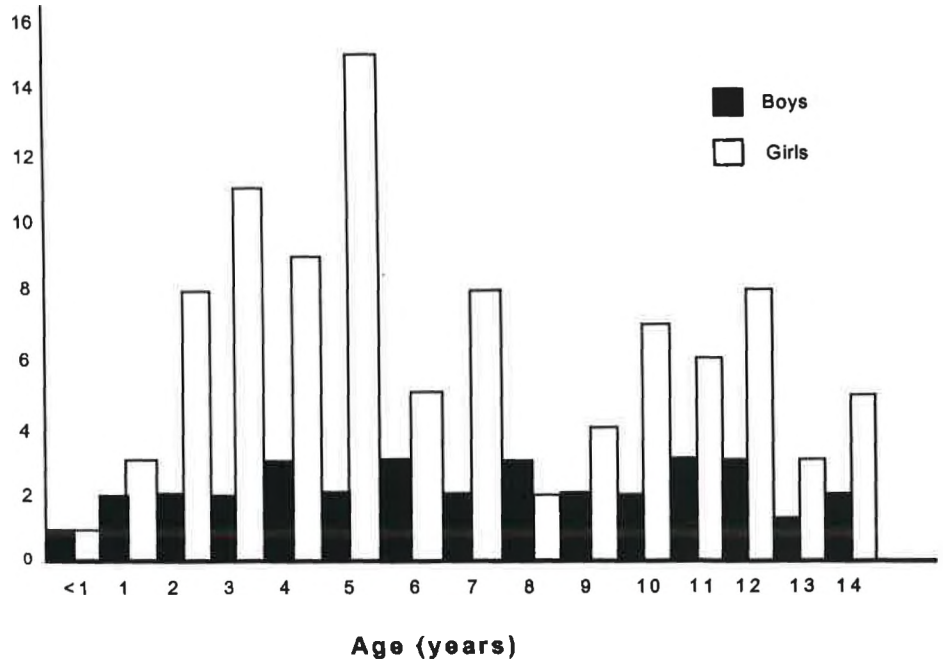

Figure 1. Distribution of total 129 nephrotic syndrome patients according to age and sex

As can be seen in Figure 1, the number of patients under the age of 6 years was 66 (51.2%), and the number over the age of 6 years was 63 (48.8%).

From clinical features with the basic criteria consisting of edema, massive proteinuria, hypoalbuminemia and hypercholesterolemia, the following nephritic symptoms were found: hematuria in 31 patients (or 24.0%), hypertension in 25 patients (19.4%), and decreased kidney function with urea concentration assessment and above normal creatinine (azotemia) in 28 patients (21.7%) (Table 1).

Table 1. Distribution of nephritic symptoms according to age

Age	Total No	Hematuria	Hypertension	Azotemia
< 6 years	66	11 (16.7%)	8 (12.1%)	5 (7.6%)
≥ 6 years	63	20 (31.7%)	17 (27.0%)	23 (36.5%)
Total	129	31 (24.0%)	25 (19.4%)	28 (21.7%)

Data in Table 1 show that nephritic symptoms were found more frequently in children over the age of 6 years than in those under the age of 6 years. This was particularly true in azotemia, which was found in 36.5 % of children over the age of 6 years as compared to 7.6 % of children under the age of 6 years. This difference was statistically significant ($p<0.05$)

Prednison management in 129 nephrotic syndrome patients showed that 108 patients (83.7%) gave good response (responders) in the form of total remission, and 21 patients (16.3%) never showed total remission (non-responders), or becoming steroid dependent/resistant who subsequently received cyclophosphamide treatment at 2 mg/kgBW (Table 2).

Table 2. Relationship between age and response to prednisone treatment

Age	Total No	Responders	Non Responders
< 6 years	66	58 (87.9%)	8 (12.1%)
≥ 6 years	63	50 (79.4%)	13 (20.6%)
Total	129	108 (83.7%)	21 (16.3%)

Table 2 shows that a greater number of non-responders were found in patients over the age of 6 years (i.e. 13/63 or 20.6%) than in those under the age of 6 years (i.e. 8/66 or 12.1%). This difference, however, was not statistically significant ($p>0.05$).

Data in Table 3 show that of all nephrotic syndrome patients, a greater percentage was under the age of 6 years (51.2%) as compared to those over the age of 6 years (48.8%). Furthermore, it is seen that the number of nephrotic syndrome steroid responders in those under the age of 6 years (i.e. 53.7%) was greater than in those over the age (i.e. 46.3%).

Data in Table 4 show that nephritic symptoms were more frequently found in non-responder than in responder patients as follow: in responder patients the number

of hematuria was 8/108 (7.4%), and hypertension or azotemia 5/108 (4.6%); whereas in non-responder patients the number of hematuria was 11/21 (52.4%), hypertension 10/21 (47.6%) and azotemia 9/21 (42.9%). Those differences was statistically significant ($p<0.05$).

Table 3. Number of nephrotic syndrome patients under and over the age of 6 years with nephrotic syndrome steroid response

	Total No	< 6 yrs	≥ 6 yrs
All nephrotic syndrome patients	129	66 (51.2%)	63 (48.8%)
nephrotic syndrome steroid responders	108	58 53.7%)	50 (46.3%)

Table 4. Relationship between steroid response and clinical features

Response	Total No	Hematuria	Hypertension	Azotemia
Responders	108	8 (7.4%)	5 (4.6%)	5 (4.6%)
Non responders	21	11 (52.4%)	10 (47.6%)	9 (42.9%)

Discussion

During the ten-year period, 129 new nephrotic syndrome patients with primary characteristic were studied. Of the 129 patients, 96 (74.4%) were males and 33 (25.6%) were females giving a male to female ratio 2.9:1. This ratio did not differ greatly from the range of 2.0:1 ratio to 2.6:1 reported by ISKDC,[11] Habib[12] and White.[13] Six years has been taken by ISKDC (1978) as the borderline in age grouping, since minimal change nephrotic syndrome (MCNS) has been found to be more frequent in children under this age (i.e., 79.6%), whereas in focal segmental glomerulosclerosis (FSGS) only 50%, and membranoproliferative glomerulonephritis (MPGN) only 2.6% .[11] In this study, the proportion of patients under the age of 6 years was 51.2%, and over the age of 6 years 48.8%. These figures were lower than those reported by ISKDC (1978) in which the number of patients under the age of 6 years was reported to be 72.3%. This difference was probably due to the fact that nephrotic syndrome patients overseas were brought to hospital for examination earlier than in Indonesia.

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Nephritic symptoms consisting of hematuria, hypertension and azotemia were more

frequently encountered in child patients over the age of 6 years than under this age (Table 1). This was in agreement with the findings of White[13] and Srivastava [14] showing that the numbers of non-minimal abnormality was greater in child patients over the age of 6 years. Also in the present study, the number of child patients over the age of 6 years and under this age with azotemia symptoms were 36.5% and 7.6% respectively ($p<0.05$). The number of patients who were steroid responders in the current study was 83.7%. ISKDC (1978) reported the number of steroid responders as being 92.6% in MCNS and 7.4% in non-MCNS, while White et al. (1970) reported the number of steroid responders to be 96.9% in MCNS and 3.1% in non MCNS. Elzonski et al.[15] reported the number of responders to be 98 % of 134 nephrotic syndrome children treated. When this was examined in patients in the current study, it was found that the number of on responders was greater in children over the age of 6 years (i.e. 8 patients or 12.1%) than under the age of 6 years (i.e. 13 or 20.6%) (Table 3).

Steroid responder nephrotic syndrome patients were frequently identical with MCNS.[16] In this study the number of steroid response nephrotic syndrome under the age of 6 years (i.e. 53.7%) was greater than over the age of 6 years. Table 4 shows that the number of patients with hematuria, hypertension or azotemia patients was found to be greater in non-responder patients. This supported the proportion that patients with nephritic symptoms are probably belong to the non-minimal group, so that it would be necessary to carry out kidney biopsy to ascertain this. In non-minimal abnormality the number of non-responders was greater, and their prognosis was also not very good.[17,18]

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