

Obesity in children with frequent relapse and steroid dependent nephrotic syndrome

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Abstract

Background Children with frequent relapse and steroid dependent nephrotic syndrome (FRNS/SDNS) will experience frequent relapse with many complications due to the disease and toxicity of steroid therapy. One of the most common complications is obesity which is associated with significant health problems in childhood and important risk factor of adult morbidity and mortality.

Objective To find out the prevalence of obesity in children with FRNS/SDNS.

Methods A cross sectional study was conducted from November 2008 until March 2009. Data were collected from the medical records of children with FRNS/SDNS treated during the period of 2000-2008. Body weight, height and body fat mass measurement was performed on the subjects. The diagnosis of obesity was based on body mass index (BMI) and body fat mass measurement.

Results Obesity was diagnosed in 10 of 43 children (23%). Most of them were 5-9 years old (58%) with male-predominance. Most patients (70%) had age of onset younger than 5 years. The median of total relapse was 7 (range 2-24) and cumulative dose of prednisone was 12,240 (range 3,490 to 44,330) mg. Time since the last dose of prednisone until the study in majority was 0 to 6 months (53%). The prevalence of obesity based on BMI was 7% while based on body fat mass was 23 (CI 95% 10 to 36) %.

Conclusion The prevalence of obesity based on body fat mass was 23%. The median BMI of obese subjects is in the 90-95th percentile. [Paediatr Indones. 2010;50:139-43].

Keywords: frequent relapse nephrotic syndrome, steroid dependent, glucocorticoid, obesity

About 60-70% children with nephrotic syndrome (NS) who have achieved remission from initial therapy will experience relapse and 50% of them become frequent relapsers.^{1,2} In managing children with primary NS, the difficult problems are the occurrence of frequent relapse, steroid dependent, and steroid resistant.^{3,4} Children with frequent relapse and steroid dependent nephrotic syndrome (FRNS/SDNS) will experience frequent relapse with many complications due to the disease as well as to the toxicity of high dose and long-term steroid therapy. One of the most common complications is obesity.⁵⁻⁸ Studies shows that the prevalence of obesity among steroid sensitive nephrotic syndrome (SSNS) subjects was 20-41%.^{9,10}

Obesity is associated with significant health problems in childhood and is an important early risk factor of adult morbidity and mortality.^{11,12} Overweight in childhood and adolescence was associated with an increased risk of morbidity from coronary heart disease (CHD).^{13,14}

Considering the morbidity of obesity, it is important to know the prevalence of obesity in children with FRNS/SDNS so that prevention, early

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detection and management could be performed. We also collected data of children with infrequent relapse nephrotic syndrome (IRNS) as a comparison.

Methods

A cross-sectional study was conducted at the Nephrology Outpatients Clinic, Department of Child Health, Cipto Mangunkusumo Hospital from November 2008 until March 2009. Data on characteristics of the subjects were collected from medical records of children with FRNS/SDNS treated during the period of 2000-2008 who fulfilled the inclusion criteria. We included patients with the onset of more than 1 year, and age at study between 5-18 years, and excluded children with diseases or abnormalities which affected the anthropometric measurement (congenital anomaly, congenital heart disease, and neoplasm), children who received other medicines which affected the anthropometric measurement, or if parents refused to participate.

Body weight, height, and body fat mass measurement was performed on the subjects. The diagnosis of obesity was based on BMI (\geq 95th percentile) and body fat mass measurement. This study was approved by the Ethics Committee, Medical School, University of Indonesia.

Results

Out of 421 patients with nephrotic syndrome registered, 73 patients were diagnosed as FRNS/SDNS. We could not recruit all children who fulfilled the inclusion criteria because only one third of them who still had routine visits at the Nephrology Outpatients Clinic. The rest had unknown address, already moved or died.

Obesity was diagnosed in 10 of 43 children with FRNS/SDNS (23%). Most of them were 5-9 years old (58%) with boys outnumbered girls (ratio 1.9:1). The age of onset was mostly younger than 5 years (70%) with a greater proportion in duration of prednisone therapy of more than 1-5 years. The median value of total relapse was 7 (range: 2 to 24). The median value of cumulative dose of prednisone was 12,240 mg (range: 3,490 to 44,330 mg). Time since the last dose of prednisone until the study was done in most of the

subjects was 0-6 months (53%) (**Table 1**).

The prevalence of obesity according to BMI was 7%, while based on body fat mass measurement was 23% (**Table 2**). Among 10 subjects who were obese, only three subjects had BMI \geq 95th percentile, and all

Table 1. Characteristics of subjects

| Characteristics | FRNS/SDNS n=43 (%) |
|--|-----------------------|
| Sex | |
| Male | 28 (65) |
| Female | 15 (35) |
| Age at study visit | |
| 5-9 years | 25 (58) |
| \geq 10 years | 18 (42) |
| Age of onset | |
| <5 years | 30 (70) |
| 5-9 years | 11 (25) |
| \geq 10 years | 2 (5) |
| Number of total relapses | |
| 2-5 | 16 (37) |
| 6-10 | 12 (28) |
| >10 | 15 (35) |
| Prednisone therapy duration | |
| \leq 12 months | 5 (12) |
| >1-5 years | 28 (65) |
| > 5 years | 10 (23) |
| Median of prednisone cumulative doses (mg) | 12,240 |
| Minimum | 3,490 |
| Maximum | 44,330 |
| Time since the last dose of prednisone until the study visit | |
| 0-6 months | 23 (53) |
| > 6 months | 20 (47) |

Table 2. Prevalence of obesity

| Method of obesity diagnosis | Obese n (%) | Not obese | total |
|-----------------------------|----------------|--------------|-------|
| BMI | 3 (7%) | 40 | 43 |
| Body fat mass | 10 (23%) | 33 | 43 |

Table 3. Distribution of obese subjects

| | Obese (n=10) |
|--|-----------------|
| Sex | |
| Male | 8 |
| Female | 2 |
| Age at study visit | |
| 5-9 years | 7 |
| \geq 10 years | 3 |
| Body mass index | |
| P 5-84 | 2 |
| P 85-94 | 5 |
| \geq P 95 | 3 |
| Time since the last dose of prednisone until the study visit | |
| 0-6 months | 10 |
| > 6 months | 0 |

obese subjects had range of time since the last dose of prednisone until the study of 0-6 months (Table 3).

Discussion

In our series the median age of patients with FRNS/SDNS was 9 (range: 5 to 18.5) years. This was not different with the results of previous studies. Foster et al^{9,15} and Leonard et al¹⁰ reported age of SSNS subjects at study visit was around 9 (SD 4 years), while Donatti et al¹⁶ and Emma et al⁶ reported in sequence 10.8 to 12.8 years and 15.3 (range : 9.6 to 21.5) years. In IRNS patients, the median of age was 10 (range: 5-18.9) years. The age of onset was mostly younger than 5 years (70%) with median 3.2 (range: 1.2 to 11) years. This was also the same with the findings of previous studies.^{6,9,10,15,16}

The median of total number of relapses was 7 (range: 2 to 24). This was similar with the findings of Leonard et al¹⁰ (six relapses), while Ruth et al¹⁷ reported that the total number of relapses in adulthood relapser group was 26 (range: 10 to 67). This was higher than ours because the number of relapse were calculated until the borderline age of childhood and adulthood.

The median duration of prednisone therapy since diagnosis at Nephrology Outpatient Clinic until the last doses was 3.2 years or 38.4 (range: 6 to 171.6) months. This result was not different from that reported by Foster et al^{9,15} and Leonard et al¹⁰. In IRNS, the duration was 1.8 (range: 3-8.5) years. The cumulative dose of prednisone (12,240 mg, range: 3,490-44,330 mg) was lower than that found by Foster et al¹⁵ (17,681 mg, range: 1,733-87,556 mg) and Leonard et al¹⁰ (15,223 mg, range: 1,524-87,556 mg). In IRNS, the median was 3,497 mg with range of 1,280 to 17,220 mg.

Time since the last dose of prednisone until the study was done in most of the subjects was 0-6 months (53%) with median of 6 months (0-11 years). This result was different from that reported by Foster et al¹⁵ and Leonard et al¹⁰. It is due to inclusion criteria differences. The previous studies included only the subjects with glucocorticoid exposure within the last 6-12 months, while this study included all patients. In IRNS, the median was 1.1 (0-8.3) years.

Anthropometry measurement showed that most subjects had BMI in the 5th-84th percentile or

well-nourished (69%), while only 7% were \geq 95th percentile or obese. The median BMI in FRNS/SDNS subjects was in the 50-75th percentile, while in IRNS was in the 25-50th percentile. Among 10 obese subjects, the median BMI was in the 90-95th percentile. Body fat mass measurement showed that majority of the subjects were healthy (51%), while 23% were obese (Figure 2).

As a comparison, we found three children that were obese among 22 children with IRNS. Mean body fat percentage in FRNS/SDNS subjects was 24%. According to body fat ranges chart, this result was included to healthy group for females aged 7-18 years, but overfat for females aged 5-6 years and all males.

The prevalence of obesity based on BMI was 7%, while based on body fat mass was 23 (CI 95% 10 to 36)%. This result (23%) was different from the previous studies which reported that the prevalence of obesity based on BMI among SSNS was 20-40%.^{9,10,15} It could be happened due to difference in the inclusion criteria used. This study included all patients, either they were in prednisone therapy or the last exposure was more than a year, so that we found less subjects with obesity. Study by Leonard et al¹⁰ included subjects who had received glucocorticoid within 12 months before the study visit, while Foster et al⁹ within the previous 6 months and also subjects who had discontinued glucocorticoid up to 6 months before the study. Other factors were the differences in geographic, race, nutrition, and sample size.

The prevalence of obesity in healthy children in Indonesia as reported by Meilany¹⁸ was 27.5% and Susanti¹⁹ was 15.3%. Susanti had studied in national and particular elementary school, while Meilany only in particular elementary school which might have difference nutrition. The higher prevalence of obesity in FRNS/SDNS compared to healthy population showed the effect of glucocorticoid exposure. In this study, the prevalence of obesity based on body fat mass was higher than based on BMI. This was also reported by Tyrrell et al²⁰ that the prevalence of obesity among school-children using BMI was 14.3%, while using the percentage body fat (PBF) was 38.3% in PBF \geq 30%.

Experts recommend BMI because it can be obtained easily and correlated strongly with body fat percentage.²¹ It is a clinically important measurement of body fat since it controls to some degree for

the influence of height, allowing comparison of obesity status across age groups.²² Recommended international BMI classification has very high specificity but the sensitivity is very low in female adolescents.²³ However, BMI does not take into account lean body mass or pubertal status²² and variation in body composition between different individuals and ethnicities.²⁰ Interpretation of assessments of overweight in children using only BMI for age and gender should include the realization that some children may have relatively high weights primarily because of high lean mass rather than high body fat levels and this is more common among male adolescents.²¹ BMI may underpredict the prevalence of excess adiposity in children with disease state.²⁴ The ability to measure actual adiposity would eliminate any potential misclassification based on BMI.²⁵

Among eight overweight subjects based on BMI, after measuring the body fat mass, we found only three who were overfat, while the rest were obese. Among 30 well-nourished subjects based on BMI, body fat measurement showed that eight were already overfat. This study suggested that obesity determination in children with FRNS/SDNS could not use BMI, especially for those who were being treated with prednisone or time since the last dose 0-6 months. Underdiagnosis of obesity by using BMI should be evaluated further.

Foster et al¹⁵ reported that subjects with SSNS had high adiposity, with a mean fat-mass-for-height-SDS 1.12 SD higher than children in the community-based reference group, but lean mass was greater in the SSNS group. Rashid et al²⁶ reviewed about growth and body composition in children with chronic kidney disease (CKD). These children may have abnormalities of their body composition (altered fat mass and lean mass according to their etiology) which may not be apparent on simple measurement of BMI. DXA data, corrected for height in children with CKD, demonstrated that BMI did not accurately reflect body composition, with patients exhibiting low lean mass with relatively high fat mass.

Studies by Foster et al¹⁵ and Rasyid et al²⁶ may explain our study which found seven from 10 subjects with obese who actually had BMI < 95th percentile. Among 11 subjects who were treated with prednisone, 10 were obese. Considering that median time to achieve remission was the end of the second week

(10-15 days), these 10 subjects might have water retention due to the disease or effect of glucocorticoid, although edema were not found clinically. From body fat mass measurement, we found that seven subjects who had BMI < 95th percentile were obese. How far the alteration of their body composition (fat mass distributions and lean mass) still needs further investigation.

Among subjects with time since the last dose more than 6 months or a year, obesity could happen in the previous time-periods. It could not be determined due to the lack of data (weight and height) in the medical records and the cross-sectional study design performed.

In conclusion, the prevalence of obesity in FRNS/SDNS subjects based on body fat mass measurement is 23%. The median BMI in FRNS/SDNS subjects is in the 50-75th percentile, while among the obese subjects is in the 90-95th percentile. Based on body fat mass measurement, all FRNS/SDNS subjects with BMI \geq 95th percentile are obese.

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