Relationship of proteinuria severity with Xerosis Cutis in children with Nephrotic Syndrome at the Haji Adam Malik Hospital

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ABSTRACT

Introduction: Proteinuria is a risk factor for the progression of Nephrotic Syndrome. Xerosis cutis is a disorder of the skin due to reduced fluid or oil content in the skin that moisture the surface of the skin layer. The three primary keys that play a role in the incidence of Xerosis Cutis are the lack of moisture-binding substances, lack of skin fat and ceramics and the latter lack of skin moisture wiring in the viable epidermis mediated by the aquaporin water channel. Reduced protein content and impaired collagen maturation, for example due to proteinuria, might influence the mechanism behind preservation skin moisture. This study aimed to determine the relationship between the severity of proteinuria and Xerosis Cutis in children with Nephrotic Syndrome.

Method: This is a cross-sectional analytic study involving 50 patients with Xerosis Cutis with Nephrotic Syndrome. Kruskal Wallis test is used to determine the association of proteinuria severity with Xerosis Cutis in children with Nephrotic Syndrome.

Result: The median value of age was 8 (3-16) years, with the most range at 6-10 years old (52%). It consists predominantly of male patients (68%). The duration of the Nephrotic Syndrome has a median value of 2 (1-7) years. Subject with +1 proteinuria (36%), +2 (32%), +3 (28%) and +4 (4%). Skin moisture level was dry (Xerosis Cutis) (36%), normal (56%), and moist (8%). There was a significant association between skin dryness and the severity of proteinuria (p = 0.002).

Conclusion: There is a significant relationship between the severity of proteinuria and Xerosis Cutis. The higher the severity of proteinuria associated with having skin dryness and thus indirectly describing the more protein wasted through urine.

INTRODUCTION

Proteinuria is a risk factor for the progressivity of Nephrotic Syndrome. Nephrotic syndrome (SN) is a clinical syndrome with many causes, characterized by increased glomerular membrane permeability with massive proteinuria that causes hypoalbuminemia and is usually accompanied by edema hypercholesterolemia. Proteinuria is associated with progressivity of glomerular damage, development of glomerulosclerosis and tubulointerstitial damage.1,2

Xerosis cutis is a disorder of the skin surface due to reduced fluid or oil content in the skin that moisture on the surface of the skin layer.3 The three primary keys that play a role in the incidence of Xerosis Cutis are the lack of moisture-binding substances commonly referred to as natural moisturizing factor (NMF), lack of skin fat defenses and ceramics and the latter lack of skin moisture wiring in the viable epidermis mediated by the aquaporin water channel.4,5

A previous study found that lower amounts of both nitrogen collagen and non-collagen in the skin of children with edema due to protein deficiency compared to healthy children. This led to impaired maturation of collagen and cross-linking of collagen fibers. Furthermore, Vasantha et al. found that the level of several amino acids (Proline, Glycine, Tyrosine) reduced in the epidermis of patients with protein deficiency conditions. For example, reduced Glycine might influence collagen synthesis as it is an integral part of the triple structure of helical collagen.6 Based on these findings, the authors were interested in researching the relationship of proteinuria severity with Xerosis Cutis in children with Nephrotic Syndrome.

METHODS

This is an observational analytic study with a cross-sectional design involving 50 patients with Nephrotic Syndrome at the Pediatric Nephrology Clinic and Dermatology and Venereology outpatient Clinic from June till December 2019. Nephrotic syndrome diagnosis based on history taking, physical examination and laboratory confirmation. Inclusion criteria include pediatric patients diagnosed with Nephrotic Syndrome in the outpatient unit of Pediatric Health Sciences (nephrology division) RSUP H. Adam Malik Medan. The exclusion criteria included patients...
who had used moisturizer, patients with other keratinization disorders such as iktiosis, and patient consumed certain drugs that influence skin moisture (cimetidine, clofazimine, tretinoin, isotretinoin, acitretin, hypocholesterolemia agents). Also, patients with metabolic diseases such as kwashiorkor, liver disorders, and zinc deficiency were excluded. A urine protein test was conducted with a simple dipstick urine test. The examination is a semi-quantitative urine test, with results of 1+ (~15 mg/dL), 2+ (~100 mg/dL), 3+ (~300 mg/dL) and 4+ (~1,000 mg/dL).2

This research was conducted after obtaining permission from the Research Ethics Commission of the Faculty of Medicine, Universitas Sumatera Utara with the number: 24/TGL/KEPK FK USU – RSUP HAM/2020; and a research license from the Directorate of Human Resources and Education Research and Development Installation of RSUP H. Adam Malik Medan with the number: LB.02.03/ XV.2.3.2/218/2020.

The raw data recording was conducted by researchers at the Nephrology Clinic of Children’s Health Sciences RSUP H. Adam Malik Medan. Raw data recording includes the patient’s identity, anamnesis, and dermatological examination, which includes skin examination using moisture checker. The study’s data were statistically analyzed using the Kruskal-Wallis test in the SPSS software to determine the relationship between the severity of proteinuria with Xerosis Cutis in children with Nephrotic Syndrome.

**RESULT**

In total, there were 50 samples enrolled in this study. The age has a median value of 8 (3-16) years. Most of the sample were within 6-10-year-old, 26 subjects (52%). Males were predominant, 34 subjects (68%). The duration of the Nephrotic Syndrome has a median value of 2 (1-7) years (Table 2).

In this study, the proteinuria severity of subjects was divided into +1 proteinuria by 18 subjects (36%), +2 by 16 subjects (32%), +3 by 14 subjects (28%) and +4 by two subjects (4%). Skin moisture level in the subject of this study was divided into; dry (Xerosis Cutis) by 18 subjects (36%), normal by 28 subjects (56%), and moist by four subjects (8%) (Table 3). There was a significant association between skin dryness and the severity of proteinuria (p = 0.002).

**DISCUSSION**

In this study, all study subjects had a median value of 8 (3-16) years, with the most age range at age 6 – 10, 26 subjects (52%). This study’s results are relevant to previous research conducted by Nilawati et al., which reported the highest age range of children with Nephrotic Syndrome in the age range of 6-10 years.3 Male study subjects 34 subjects (68%) and women as many as 16 subjects (32%). Fadilah (2018) also mentioned the proportion of boys

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**Table 1. Interpretation Moisture Checker**

| Body site            | Dry  | Normal | Moist |
|----------------------|------|--------|-------|
| Forehead             | < 37%| 37 – 54%| > 54% |
| Around the eyes      | < 40%| 40 – 54%| > 54% |
| Medial side of the arm | < 37%| 37 – 45%| > 45% |

**Table 2. Characteristics of the Sample**

| Characteristics of the respondent | Median (minimum-maximum) | n (50) | Percentage |
|-----------------------------------|---------------------------|--------|------------|
| Age (years)                       | 8 (3-16)*                 |        |            |
| 1 - 5 years old                   | 12                        | 24%    |            |
| 6 – 10 years old                  | 26                        | 52%    |            |
| 11 – 15 years old                 | 10                        | 20%    |            |
| ≥ 16 years old                    | 2                         | 4%     |            |

| Gender                            |                          |        |            |
|-----------------------------------|---------------------------|--------|------------|
| Male                              | 34                        | 68%    |            |
| Female                            | 16                        | 32%    |            |

| Duration of Nephrotic Syndrome (years) | 2 (1-7) |

* Data is presented in the form of median and minimum-maximum values (data not normally distributed)

**Table 3. Overview of Proteinuria Characteristics and Skin Moisture**

| Variable              | n (50) | Percentage |
|-----------------------|--------|------------|
| Proteinuria           |        |            |
| +1                    | 18     | 36%        |
| +2                    | 16     | 32%        |
| +3                    | 14     | 28%        |
| +4                    | 2      | 4%         |

| Skin Moisture         |        |            |
|-----------------------|--------|------------|
| Dry                   | 18     | 36%        |
| Normal                | 28     | 56%        |
| Wet                   | 4      | 8%         |
with Nephrotic Syndrome at 68.57% while girls by 31.43%. The results of this study are relevant to previous studies conducted by Simandjuntak et al., which reported 67.5% of male subjects with Nephrotic Syndrome. Duration of the Nephrotic Syndrome has a median value of 2 (1-7) years. Raisania et al. reported that the mean duration of suffering from Nephrotic Syndrome was 22.71 ± 17.83 months. Arif et al. also reported that 87.5% of children had Nephrotic Syndrome with a time <5 years. The severity of proteinuria in subject +1 was 18 subjects (36%), +2 was 16 subjects (32%), +3 was 14 subjects (28%) and +4 was 2 subjects (4%). This study’s results are relevant to previous research conducted by Bushara (2006), which showed that 52.7% of patients with the Nephrotic Syndrome had proteinuria <3+ and 47.3% had proteinuria ≥3 +. The level of moisture in the skin of the research subjects classified as dry (Xerosis Cutis) was 18 subjects (36%), normal as many as 28 subjects (56%) and moist/wet as many as 4 subjects (8%). The results of this study are relevant to the research conducted by Simandjuntak et al who reported the percentage of the moisture level of the skin of children with dry Nephrotic Syndrome as much as 40% of the subjects.

According to previous knowledge, Nephrotic Syndrome defined as the presence of massive proteinuria (> 40 mg / m2LPB / hour or protein / creatinine ratio in urine > 2 mg / mg or dipstick ≥ 2+), hypoalbuminemia ≤ 2.5 g / dL, edema, and hypercholesterolemia. These conditions can certainly cause changes in the skin structure, one of which is the stratum corneum. The stratum corneum is a non-nucleated cell containing various protein (prophylagrin, filaggrin and keratohyalin granules). Also, there are also natural moisturizing factors (Natural Moisturizing Factors). NMF is produced by lamellar granules, which will absorb water. NMF contains lipids and proteins that form a mosaic barrier. These materials will protect the skin and prevent the loss of moisture. NMF is also able to absorb water, which will increase the moisture content of the skin. The results of this study found that there was a significant relationship of skin dryness based and severity of proteinuria (p = 0.002). Thus, it can be concluded that the higher the severity of proteinuria, the higher the level of dryness of the skin and the greater the severity of proteinuria in children with Nephrotic Syndrome, then indirectly describe the more protein that is wasted through urine. Skin lesions can be a source of infection, which will aggravate the primary disease. Therefore, patients suffering from dry skin need emollients to moisturize their skin. Patients also need to be informed not to shower with too much soap as it will irritate the skin.

CONCLUSION

There is a significant association between the severity of proteinuria and Xerosis Cutis. The higher the severity of proteinuria, the higher the level of Xerosis Cutis in the skin of children with Nephrotic Syndrome.

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AUTHOR CONTRIBUTION

All authors have contributed to this research process, including preparation, data gathering and analysis, drafting and approval for publication of this manuscript.

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CONFLICT OF INTEREST

The authors declare no conflict of interest regarding the publication of this article.

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