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ORIGINAL ARTICLE

Significance of Serum Hemopexin as A Prognostic Marker in Children with Idiopathic Nephrotic Syndrome.

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ABSTRACT

Background: Idiopathic nephrotic syndrome (INS) is the most common form of podocytopathy in children. Although the dramatic response to steroid therapy, steroid resistance occurs in 10% to 30% of cases. Hemopexin is a plasma β-1 glycoprotein circulating in serum. Hemopexin has been discovered to influence glomerular basement membrane permeability to albumin. This study aimed to examine the relation between plasma hemopexin (Hx) and the course of idiopathic nephrotic syndrome and assess the relation between plasma hemopexin levels and steroid insensitivity. **Patient and methods**: This a case control study, included 39 children which were allocated to two groups A and B, in addition to the control group C. Group (A) included 13 newly diagnosed patients with steroid-resistant nephrotic syndrome (SRNS). Group (B) included 13 new patients with steroid-sensitive nephrotic syndrome (SSNS). The control group (Group C) included 13 normal children. All participants underwent full history taking, clinical examination, laboratory investigations, then whole blood samples were taken to estimate plasma hemopexin levels by ELISA technique. The statistical analysis done to interpret the results. **Results**: The plasma hemopexin level was higher in steroid resistant cases than in the steroid sensitive with a Signiant difference<0.001.**Conclusions**: Serum hemopexin level gives a predictive information about the course of INS, and produces a guide for nephrologists to prevent excessive glucocorticoid-induced toxicity and earlier switching to more effective substitute therapy.

Keywords: idiopathic nephrotic syndrome (INS), hemopexin (Hx), steroid-resistant nephrotic syndrome.

INTRODUCTION

Idiopathic nephrotic syndrome (INS) is a major glomerular condition in Egyptian children. 30% of Egyptian children with INS undergo resistance to treatment with steroids. Nephrotic syndrome is responsible for two hundred forty-two deaths in Egyptian children annually. In this regard, Egypt ranks as the second country in the world regarding NS deaths. Japan came the first country in NS mortality, with a total of 447 deaths per year. The mortality rate in the United States reached 153 deaths per year [1].

Minimal change disease (MCD) has been found to be the most prevalent type of nephrotic syndrome (NS). Ninety per cent of patient with MCD occurs in <10 years old, and 50% of them less than 8 years old [2]. The main clinical manifestations include massive proteinuria, hypoalbuminemia, hypercoagulability, an imbalance of electrolytes and fluids, and increased tendency to infection. The essential pathological finding is foot processes thinning

and shortening in podocytes of the glomeruli, lack of immune complex accumulation or basement membrane injury [3]. MCD is known for its dramatic reaction to steroids (within 4 weeks); nevertheless, resistance to immunosuppressive therapy may occur in 10% of cases and may progress to end-stage renal disease (ESRD) [4].

The most recent theory is the "two-hit" theory. This theory supposes that damage to podocytes is a complex process that includes two hits. The initial hit is the activation of podocytes and enhanced CD80 expression. Many allergens, including bacterial and viral factors, lead to the production of T-linked cytokines and the stimulation of podocytes. CD80 expression is a marker for podocyte injury, hence increased permeability to protein. The second hit is regulatory T-cell dysfunction. T-regulatory cells (T-regs) normally recover podocyte stimulation. IL-10, CTLA-4, and TGF-β all are secondary messengers in the action of T regulatory cells. The regulatory T-cell dysfunction, upregulate CD80, resulting in INS [5,6]. The causes of proteinuria in INS are complex and not completely understood, so new hypotheses introduced to explain these states [7]. One hypothesis is that dysfunctional T lymphocytes release circulating permeability factors that are responsible for the occurrence of proteinuria in INS patients. The cytokine levels in the serum of children with INS are pathogenic markers. IL-8 and IL-13 are mostly suggested. Despite these, many of these hypotheses are inconclusive [8–10].

Hemopexin (Hx) is encoded by a gene located on chromosome 11 at pp. 5.4 to 15. Hx is a plasma β-1 glycoprotein circulating in serum. Hx has a molecular weight of 60 kDa [11,12]. It is a single polypeptide chain synthesized mainly in hepatocytes. It contains a disulfide bond and a heme moiety. Hx involves in the homeostasis of iron. Heme molecule is released in the serum and reaches the liver to be catalyzed with the addition of iron stores in the liver [13].

The Hx remains in the circulation for 7 days. The serum concentration of hemopexin is related to hemoglobin concentration; low concentrations are indicative of severe hemolysis, while the absence of Hx is a marker of chronic liver disease or malnutrition. Normal level of Hx in urine is 2 mg/L. The urinary Hx (uHx) concentration increases with glomerular proteinuria in patients with diabetes mellitus. [14]. Urinary Hx levels also increase in other conditions, e.g., some psychiatric disorders, neuromuscular diseases, and cancer [15–17]. The serine protease activity of hemopexin includes anti-inflammatory effects, pro-inflammatory effects, inhibition of granulocyte necrosis, and cell integrity [18]. Recently, hemopexin has been discovered to affect glomerular membrane permeability, hence the occurrence of proteinuria [12]. This study depends on the experimental studies that found increased serum level of hemopexin in cases of nephrotic syndrome and some nephrologists attribute this increase to influence the glomerular membrane permeability and the occurrence of the disease [12].

The aim of this study was to find if there`s a relation between serum hemopexin level and the steroid resistance in cases of INS.

PATIENTS AND METHODS

This case control investigation was carried out on 39 children attending the nephrology unit and clinic of the pediatric department at Zagazig University Hospital from July 2023 to December 2023. Informed consent was obtained from all parents. The approval for performing the study was obtained from the pediatric departments of Zagazig University Hospitals after receiving approval from the Institutional Review Board (N10596-21-3-2023). The study was carried out according to the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

The age of children were 2-14 years of both genders. The full criteria of nephrotic syndrome were included in this study. Patients were receiving treatment with 1-2 mg/kg of corticosteroids.

The following criteria were excluded: age <2 years or >14 years. Children with hereditary or

congenital NS, severe protein-energy malnutrition.

Patients were allocated into two groups: A and B. Group (A) included 13 newly diagnosed patients with steroid-resistant nephrotic syndrome (SRNS) [19] (5 males and 8 females). Group (B) included 13 new cases of steroid-sensitive nephrotic syndrome (SSNS) [19] (5 males and 8 females). The control group(C) included 13 normal children from those attending general paediatric clinics.

All patients were subjected to a full history (age, sex, and age at the onset of INS) and thorough clinical assessment, with a focus on vital data and all systems, anthropometric data for all recruited participants. Data about medical treatment (type and dose), disease presentation, and complications were recorded.

Radiological assessment: Abdominal ultrasonography and plain X-ray chest imaging were performed for all patients.

Biochemical assessment: All laboratory tests were assessed only once at case hospital admission, according to the routine lists of Zagazig University laboratories: complete blood count (CBC), C-reactive protein, total serum albumin, serum protein, total urinary protein level, total cholesterol, and urine analysis. In all children under study, renal function tests were normal, while inflammatory markers were negative. The estimated glomerular filtration rate (eGFR) was estimated following the Schwartz formula [20]. All the collected blood samples were subjected to biochemical analysis immediately after collection.

The first morning urine samples were utilized for urinary protein/creatinine ratio (uPCR) assessment. A uPCR> 2 (2 mg/mg) was considered as a marker of proteinuria in nephrotic syndrome [21]. The Guidelines for the International Study of Kidney Disease in Pediatrics define complete remission as a decrease in proteinuria to < 0.2 mg/mg uPCR or null dipstick findings in three consecutive days.

Hemopexin concentrations in serum (sHx) were assessed by enzyme-linked immunosorbent assay (ELISA) utilizing commercial kits following the manufacturer's instructions.

Statistical analysis:

The acquired data was analysed utilizing the Statistical Package for Social Services (SPSS) version 24. The data was arranged in graphs and tables. Continuous quantitative variables, such as age, were presented as the mean ± SD and median (range), while categorical qualitative variables were presented as absolute and relative frequencies. The P value less than 0.05 was significant, and P value less than 0.001 was highly significant.

We utilized the following tests in this study: the Chi-square test, one-way ANOVA, Mann Whitney test, Monte Carlo test, correlation analysis (using Spearman/Pearson's method), and receiver operating characteristic (ROC).

RESULTS

Table (2): There were significant differences between groups A and B regarding the incidence of edema. Table (3): Significant differences between groups A and B regarding urine analysis (dipstick), total cholesterol, serum albumin, and uPCR. Table (4): The plasma hemopexin level in group A was 107.6 ng/ml, but the levels in groups B and C were 51.2 ng/ml and 32.2 ng/ml, respectively, with significant differences. Table (5): The best cut of value of plasma hemopexin for the diagnosis of SRNS was ≥100 ng/ml. Table (6): There were significant positive correlations between plasma hemopexin levels and proteinuria, the protein/creatinine ratio, and serum cholesterol. However, there was a significant negative correlation between plasma hemopexin and serum albumin.

Table (1): Comparison between the studied groups regarding sex, age, weight, height, BMI.

	Group A N=13 (%)	Group B N=13 (%)	Group C N=13 (%)	χ^2	P
Sex: Female Male	 5 (38.5%) 8 (61.5%)	 5 (38.5%) 8 (61.5%)	 6 (46%) 7 (54%)	0.69	0.621
	Mean ± SD	Mean ± SD	Mean ± SD	F	P
Age (year)	7.27 ± 1.81	7.54 ± 1.65	6.74 ± 1.81	0.449	0.244
Weight (Kg)	24.69±5.472	23.3±8.99	17.24 ± 2.9	0.449	0.244
Height (cm)	115.79±27.8	123.67±30.11	120.67±30.11	0.95	0.096
BMI	14.39±5.48	14.18±5.45	15.62±11.1	0.95	0.096

χ^2 Chi square test F One way ANOVA test Z Mann Whitney test

Table (2): Comparison between the studied groups regarding clinical picture and complications.

	Group A N=13 (%)	Group B N=13 (%)	χ^2	P
Edema: Absent Present	 2 (15.2%) 11 (84.8%)	 13(100%) 0 (0%)	46.552	<0.001**
Blood pressure: Normal High	 12 (92.4%) 1 (7.6%)	 12 (92.4%) 1 (7.6%)	Fisher	>0.5
Hematuria: Absent Present	 12 (92.4%) 1 (7.6%)	 13 (100%) 0 (0%)	Fisher	>0.5
Renal failure: Absent Present	 13 (100%) 0 (0%)	 13(100%) 0 (0%)	Fisher	>0.5
Thrombosis (no)	0 (0%)	0 (0%)	0	>0.5
Infection: No infection Chest infection Urinary tract infection	 11 (84.6%) 1(7.6%) 1 (7.6%)	 11 (84.6%) 0 (0%) 2 (15.2%)	MC	>0.5

**p ≤0.001 is statistically highly significant χ^2 Chi square test

Table (3): Comparison between the studied groups regarding laboratory data:

	Group A N=13 (%)	Group B N=13 (%)	Group C N=13 (%)	F	P
	Mean ±SD	Mean ± SD	Mean ± SD		
Albumin (g/dl)	2.57 ± 0.72	3.27 ± 0.37	4.29 ± 0.38	100.38	<0.001**
LSD	P_2<0.001**	P_1<0.001**	P_3<0.001**		
Cholesterol (mg/dl)	259.04 ±18.26	199.63± 22.17	99.0 ± 12.34	223.69	<0.001**
LSD	P_2 0.001**	P_1<0.001**	P_3<0.001**		
Platelet (10^3/mm^3)	229.56 ±69.90	232.11±51.60	228.48±58.52	0.125	0.871
WBCs (10^3/mm^3)	7.89 ± 1.29	7.88 ± 1.28	8.37± 1.11	1.457	0.212
Hemoglobin (g/dl)	11.16 ± 073	11.19± 0.9	11.07 ± 1.14	0.092	0.811
CRP(mg/L)	3.17 ±0.15	2.75 ±0.10	1.75 ±.11	2.121	0.112

Creatinine (mg/dl)	0.44 ± 0.12	0.42 ± 0.14	0.44 ± 0.16	0.296	0.7452
Urea (mg/dl)	24.04 ± 1.07	24.32 ± 1.26	23.66 ±2.61	0.926	0.401
Protein/creatinine ratio	7.0±2.97 (4.9–9.7)	1.81±.0.06 (1.5–1.9)	0.18±0.01	263.054	<0.001**
LSD	P_2<0.001**	P_1<0.001**	P_3 0.117		
Urine analysis (dip stick) Negative Trace 2+ 3+ 4+	 0 (0%) 0 (0%) 6(46.2%) 5(38.4%) 2(15.3%)	 11(84.6%) 2 (15.2%) 0 (0%) 0 (0%) 0(0%)		χ^2 46.202	<0.001**

F One way ANOVA test LSD Fisher least significant difference **p ≤0.001 is statistically highly significant *p <0.05 is statistically significant p1 difference between groups A and B p2 difference between groups B and C p3 difference between groups A and C χ^2 Chi square for trend te

Table (4): Comparison between the studied groups regarding Plasma Hemopexin**:**

	Group A N=13 (%)	Group B N=13 (%)	Group C N=13 (%)	F	P
	Mean ±SD	Mean ± SD	Mean ± SD		
Hemopexin Plasma level (ng/ml)	107.6	51.2	32.2	553.699	<0.001**
LSD	P_1<0.001**	P_2<0.001**	P_3<0.001**		

F One way ANOVA test LSD Fisher least significant difference **p ≤0.001 is statistically highly significant *p <0.05 is statistically significant p1 difference between groups A and B p2 difference between groups B and C p3 difference between groups A and C

Table (5): Performance of plasma Hemopexin in diagnosis of steroid-resistant nephrotic syndrome.

Cutoff	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy	P
≥100	0.95	97%	87%	85.7%	95%	94%	<0.001**

**p ≤0.001 is statistically highly significant PPV positive predictive value
NPV negative predictive value AUC area under curve.

Table (6): Correlation between plasma Hemopexin and the studied parameters among patients with nephrotic syndrome.

	R	P
Age at onset (year)	0.214	0.12
Proteinuria	0.793	<0.001**
Creatinine (mg/dl)	0.085	0.541
Protein/creatinine ratio	0.789	<0.001**
Urea (mg/dl)	-0.054	0.635
Albumin (g/dl)	-0.441	<0.001**
Cholesterol (mg/dl)	0.733	<0.001**
Platelet (10^3/mm^3)	-0.117	0.4
WBCs (10^3/mm^3)	0.096	0.49
Hemoglobin (g/dl)	0.028	0.838

r Pearson correlation coefficient §Spearman rank correlation coefficient
*p <0.05 is statistically significant **p≤0.001 is statistically highly significant

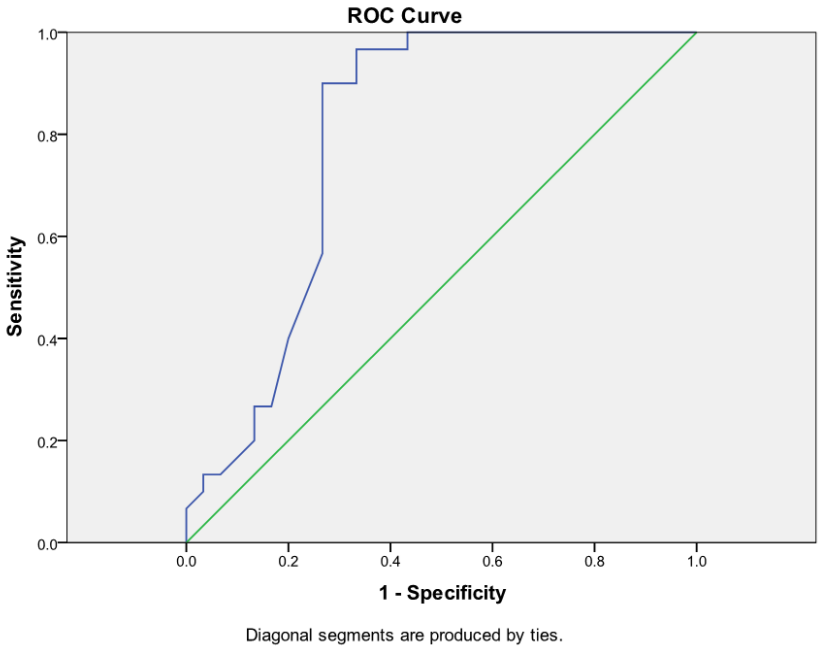

Figure (1): ROC curve showing performance of plasma Hemopexin in diagnosis of steroid resistant nephrotic syndrome

DISCUSSION

The present study reported substantial variance between the studied groups concerning plasma hemopexin, with a statistically significant positive correlation between plasma hemopexin among patients with NS and all cases of proteinuria (by dipstick), protein–creatinine ratio, and serum cholesterol. However, there was no substantial correlation between plasma hemopexin among patients with NS and age of disease onset, WBC count, hemoglobin, platelet count, urea, or creatinine. Data on this subject in the literature are scarce. Our findings were similar to those of Pukajło-Marczyk [12]. The findings of Bakker et al. [22] disagreed with our observations. They found lower mean plasma Hx titres in MCD relapse patients than in MCD remission patients ($p < 0.01$). Some circulating factors involved in the development of NS in children have been identified including hemopexin. These factors are not related to mutations in genes encoding basal lamina or podocyte proteins [2,23]. Experimental studie revealed Hx in its inactive form in the serum. They also found the active form of Hx. This form has serine protease properties that influence podocyte function and structure [23]. The application of recombinant Hx to one kidney causes reversible, substantial proteinuria and architectural abnormalities, as demonstrated by experimental studies in rats. A similar observation could be made in INS, in addition to the loss of negative charge in the glomerular filtration barrier (GFB) [22].

Lennon et al. [24] showed that Hx increases the nephrin-dependent rearrangement of actin in the podocyte cytoskeleton and reduces the glycocalyx. Preincubation with plasma from healthy individuals dramatically inhibited the degree of cytoskeletal rearrangement in podocytes following Hx treatment. This finding raises the possibility that the normal plasma component has a protective effect against active Hx, and this protection is lost in cases of INS. These differences may be attributed to the use of different techniques for Hx assessment. They used the rocket electrophoresis technique to measure the plasma Hx titre by employing anti-Hx IgG. The plasma Hx concentration may be underestimated due to changes in the Hx molecular configuration. There may also be changes in plasma Hx levels with age; i.e., this value accounts for approximately 20% (0.4 g/L) of plasma Hx in newborns and 80% (1.5 g/L) of

plasma Hx in children [24,25]. Other doubts, including the absence of data about the time at which samples were collected at the time of reaching steroid sensitivity. The authors also revealed a large increase in Hx by evaluating ecto-apyrase expression. Incubation of kidney sections in plasma from children with NS results in glomerular extracellular damage, and ecto-pyrase is an indicator of this damage. On the other hand, following the use of plasma from MCD patients in remission or healthy individuals, protease activity was not detected. The increase in Hx concentration in the MCD diet group may be explained by the fact that Hx is primarily generated in hepatocytes as an acute-phase protein. The activation of postinflammatory cytokines, particularly IL-1 and IL-6, may stimulate the inflammatory process [26].

In the present study, the relationship between C-reactive protein and Hx was not significant. This result does not exclude the possibility of hepatic synthesis of Hx or the role of other inflammatory cytokines, e.g., IL-6. IL-6 levels increase during INS relapse in both adults and children [19,20]. Kobayashi and Sleem [23] provided evidence of partial release of Hx into the circulation from glomerular mesangial cells. Following previous treatment with TNF-alpha, the supernatant of mesangial cells from normal individuals contained Hx. Local Hx synthesis in these mesangial cells may have direct effects on podocytes. Previous experimental studies have confirmed the effect of Hx on the permeability of GFB. Thus, an association between the tested proteinuria and glycoproteins could be expected. However, such a correlation could not be detected. This could be attributed to the small sample size of the patient group. Krikken et al. [27] emphasized the link between proteinuria and Hx. The investigation included 557 recipients of renal transplants at risk of graft loss. Proteinuria was shown to be considerably greater in patients with increased plasma Hx. They additionally determined that transplanted kidneys failed more quickly than in patients with lower levels. Hx is an independent risk factor for kidney allograft loss. The increasing permeability of GFB to proteins has been identified as a controllable factor in the progression of chronic kidney disease [28]. Similar observations were reported by Pukajło-Marczyk [12]. Other researchers have investigated the correlation of INS children with the circulating factor IL-13, which is considered a significant enhancer of glomerular permeability in MCD [20].

Research on Hx and other biochemical markers of nephrotic syndrome revealed nonsignificant associations in the whole patient group [12]. This observation may be due to the small sample size and interactions among cytokines. A relationship between Hx and the cytokine network was proven. Several investigations on inflammatory conditions, including sepsis, have validated this relationship [29]. Similar findings were presented by Kapojos et al. [30].

CONCLUSION AND RECOMMENDATION

In this study, we found higher level of serum hemopexin in the steroid resistant cases than those steroid sensitive. We can give an information about the importance of hemopexin as a predictive marker of INS but owing to the small size of this study and it is also a single center study, we recommend performing long-term prospective study concerning its role in the prediction of the disease. The dynamics of hemopexin (Hx) concentrations must be compared at the first onset of the disease and then at each subsequent relapse in every patient. The results are then analysed in groups depending on the number of relapses.

REFRENCES

1. Meena P, Renuga S. Assess the knowledge on nephrotic syndrome among mother of under five children at SMCH. Age. 2019;21:31–40.

2. Cara-Fuentes G, Clapp WL, Johnson RJ, Garin EH. Pathogenesis of proteinuria in idiopathic minimal change disease: molecular mechanisms. Pediatr Nephrol. 2016;31:2179–89.

3. Eddy AA, Symons JM. Nephrotic syndrome in childhood. Lancet. 2003;362:629–39.

4. Noone DG, Iijima K, Parekh R. Idiopathic nephrotic syndrome in children. Lancet. 2018;392:61–74.

5. Reiser J, Mundel P. Danger signalling by glomerular podocytes defines a novel function of inducible B7-1 in the pathogenesis of nephrotic syndrome. J Am Soc Nephrol. 2004;15:2246–8.
6. Shimada M, Araya C, Rivard C, Ishimoto T, Johnson RJ, Garin EH. Minimal change disease: a "two-hit" podocyte immune disorder? Pediatr Nephrol. 2011;26:645–9.
7. Kim SH, Park SJ, Han KH, Kronbichler A, Saleem MA, Oh J, et al. Pathogenesis of minimal change nephrotic syndrome: an immunological concept. Korean J Pediatr. 2016;59:205–11.
8. Lai K-W, Wei C-L, Tan L-K, Tan P-H, Chiang GSC, Lee CGL, et al. Overexpression of interleukin-13 induces minimal-change-like nephropathy in rats. J Am Soc Nephrol. 2007;18:1476–85.
9. Souto MFO, Teixeira AL, Russo RC, Penido M-GMG, Silveira KD, Teixeira MM, et al. Immune mediators in idiopathic nephrotic syndrome: evidence for a relation between interleukin 8 and proteinuria. Pediatr Res. 2008;64:637–42.
10. Ahmed HM, Botrous OE, Khattab R, Abdallah AM. Urinary Interleukin-8 as a Biomarker for Steroid Resistance in Childhood Onset Nephrotic Syndrome. GEGET. 2019;14:90–5.
11. Purohit S, Piani F, Ordoñez FA, de Lucas-Collantes C, Bauer C, Cara-Fuentes G. Molecular Mechanisms of Proteinuria in Minimal Change Disease. Front Med (Lausanne). 2021;8:761600.
12. Pukajło-Marczyk A, Zwolińska D. Involvement of Hemopexin in the Pathogenesis of Proteinuria in Children with Idiopathic Nephrotic Syndrome. J Clin Med. 2021;10:3160.
13. Lechuga GC, Napoleão-Pêgo P, Morel CM, Provance DW, De-Simone SG. New Insights into Hemopexin-Binding to Hemin and Hemoglobin. Int J Mol Sci. 2022;23:3789.
14. Dutt S, Hamza I, Bartnikas TB. Molecular Mechanisms of Iron and Heme Metabolism. Annu Rev Nutr. 2022;42:311–35.
15. Chen C-C, Lu Y-C, Chen Y-W, Lee W-L, Lu C-H, Chen Y-H, et al. Hemopexin is upregulated in plasma from type 1 diabetes mellitus patients: Role of glucose-induced ROS. J Proteomics. 2012;75:3760–77.
16. Dowling P, Holland A, Ohlendieck K. Mass Spectrometry-Based Identification of Muscle-Associated and Muscle-Derived Proteomic Biomarkers of Dystrophinopathies. J Neuromuscul Dis. 2014;1:15–40.
17. Wang Y, Yang P, Yan Z, Liu Z, Ma Q, Zhang Z, et al. The Relationship between Erythrocytes and Diabetes Mellitus. J Diabetes Res. 2021;2021:6656062.
18. Chiabrando D, Vinchi F, Fiorito V, Mercurio S, Tolosano E. Heme in pathophysiology: a matter of scavenging, metabolism and trafficking across cell membranes. Front Pharmacol. 2014;5:61.
19. Moustafa B, Moselhy S, Rabie M, Hammad A, Youssef D, Shouman M, et al. Egyptian pediatric clinical practice adapted guidelines: evidence-based [2] steroid-resistant nephrotic syndrome (SRNS) 2022. Egyptian Pediatric Association Gazette. 2023;71:12.
20. Schwartz GJ, Muñoz A, Schneider MF, Mak RH, Kaskel F, Warady BA, et al. New equations to estimate GFR in children with CKD. J Am Soc Nephrol. 2009;20:629–37.
21. Giliberti M, Mitrotti A, Gesualdo L. Podocytes: The Role of Lysosomes in the Development of Nephrotic Syndrome. Am J Pathol. 2020;190:1172–4.
22. Bakker WW, van Dael CML, Pierik LJWM, van Wijk JAE, Nauta J, Borghuis T, et al. Altered activity of plasma hemopexin in patients with minimal change disease in relapse. Pediatr Nephrol.
23. Kobayashi Y, Saleem MA. Hemopexin in Minimal Change Nephrotic Syndrome. In: Kaneko K, editor. Molecular Mechanisms in the Pathogenesis of Idiopathic Nephrotic Syndrome [Internet]. Tokyo: Springer Japan; 2016 [cited 2024 Mar 27]. p. 13–23.005;20:1410–5. Available from: https://doi.org/10.1007/978-4-431-55270-3_2
24. Lennon R, Singh A, Welsh GI, Coward RJ, Satchell S, Ni L, et al. Hemopexin induces nephrin-dependent reorganization of the actin cytoskeleton in podocytes. J Am Soc Nephrol. 2008; 19:2140–9.
25. Clerc F, Reiding KR, Jansen BC, Kammeijer GSM, Bondt A, Wuhrer M. Human plasma protein N-glycosylation. Glycoconj J. 2016; 33:309–43.
26. Ray EC, Rondon-Berrios H, Boyd CR, Kleyman TR. Sodium retention and volume expansion in nephrotic syndrome: implications for hypertension. Adv Chronic Kidney Dis. 2015;22:179–84.
27. Krikken JA, van Ree RM, Klooster A, Seelen MA, Borghuis T, Lems SPM, et al. High plasma hemopexin activity is an independent risk factor for late graft failure in renal transplant recipients. Transpl Int. 2010;23:805–12.
28. Nickavar A, Valavi E, Safaeian B, Amoori P, Moosavian M. Predictive Value of Serum Interleukins in Children with Idiopathic Nephrotic Syndrome. Iran J Allergy Asthma Immunol. 2020;19(6):632-9.

29. Lin T, Kwak YH, Sammy F, He P, Thundivalappil S, Sun G, et al. Synergistic inflammation is induced by blood degradation products with microbial Toll-like receptor agonists and is blocked by hemopexin. J Infect Dis. 2010;202:624–32.

30. Kapojos JJ, van den Berg A, van Goor H, te Loo MWM, Poelstra K, Borghuis T, et al. Production of hemopexin by TNF-alpha stimulated human mesangial cells. Kidney Int. 2003;63:1681–6.

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