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Assessment of Fibroblast Growth Factor- 23 and Klotho Protein in Children with Steroid-Sensitive Nephrotic Syndrome and Steroid-Resistance Nephrotic Syndrome

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Abstract

Idiopathic nephrotic syndrome is a common disease that affects children's kidneys and occurs due to a specific defect in the glomeruli, which leads to the leakage of protein into urine in large quantities. Fibroblast growth factor-23 (FGF-23), produced by bone, is essential for controlling the metabolism of 1,25-dihydroxy vitamin D and phosphate, but it also requires the Klotho co-receptor to perform its function. Therefore, the purpose of this study was to evaluate whether FGF-23 can be used as a biomarker to determine the likelihood of recurrent relapse as well as to differentiate between steroid-sensitive nephrotic syndrome (SSNS) and steroid-resistant nephrotic syndrome (SRNS) treated with glucocorticosteroids. In this cross-sectional study, 85 patients with idiopathic nephrotic syndrome were divided into four groups: Out of 50 children included in this study with (SSNS) were grouped in the first group (20) in relapse and the second (30) in remission, in addition to 35 child had (SRNS) were divided as: the third group of (20) in the relapse phase and the fourth group of (15) in the remission phase, while the control group included 40 healthy children. The fibroblast growth factor (FGF-23) levels and its co-receptor Klotho were measured in these patients using an ELISA kit. Our results revealed that serum levels of FGF-23 were significantly elevated in steroid-sensitive NS with a mean of (51.73 ng/L) in relapse and (16.49 ng/L) in remission, while for the steroid-resistant groups (67.25 ng/L) in relapse and (24.66 ng/L) in remission, compared with the control group with a mean of 7.73 ng/L ($P < 0.0001$). At the same time, Klotho concentrations were decreased for all patient groups compared with the control group. Hence, FGF-23 serum level is a potential biomarker to identify patients with frequent relapses at a cutoff value (16.055 ng/L). While its ability to distinguish between SSNS and SRNS patients was lower at a cut-off value of (20.00 ng/L).

Keywords: fibroblast growth factor-23, klotho, idiopathic nephrotic syndrome.

Introduction

Idiopathic nephrotic syndrome (INS) indicates unclear course of disease progression. commonly affects children in the age group 2-6 years with a slight preponderance of males[(1)]. The most common type of idiopathic nephrotic syndrome is Minimal Change Disease (MCD), and in this type, there is a good response to treatment with glucocorticoids, this condition is known as a steroid-sensitized nephrotic syndrome (SSNS). On the other hand, the disease sometimes appears in the form of repeated and successive attacks (Frequent relapse), and these conditions dictate that it must be treated with steroids, despite all the side effects resulting from the use of the drug[(2)]. In more than 90% of children with nephrotic syndrome, the cause of its occurrence is unknown, and it is called (primary nephrotic syndrome or nephrotic syndrome of unknown cause).

Prednisolone is the standard treatment for motivating remission in nephrotic syndrome. The majority of children who respond to this medicine (SSNS), the bulge and protein in the urine disappears within a few weeks (the disappearance of protein is classified as remission)[(3)]. For a small group of children (SRNS) who do not respond to steroid treatment, further investigations are performed, such as a kidney biopsy. The alternative drugs used for these patients are cyclophosphamide, cyclosporine, mycophenolate mofetil, and others[(4)]. FGF-23 has a critical role in controlling phosphate homeostasis in the skeleton, where it is primarily generated by osteocytes and osteoblasts. Not too long after FGF-23 was first identified as a possible phosphaturic hormone, a substantial correlation between FGF-23 and vitamin D metabolism was discovered[(5)].

FGF-23 level rises in the early stages of kidney failure, suggesting that it is a sensitive marker of abnormal phosphate processing in CKD patients[6]. The kidneys' fibroblast growth factor receptor-1 (FGFR1) can bind to FGF-23, but it also needs the co-receptor klotho to function[7]. Research has demonstrated that decreased levels of Klotho protein, accompanied by a rise in FGF-23 levels, may serve as a biomarker for kidney injury. Furthermore, its ability could serve as a risk factor for cardiovascular disease (CVD) [8,9]. A decreased incidence of osteoporosis is associated with a greater serum Klotho level [10]. It has been demonstrated that a Klotho loss can enhance many central nervous system-related neuropathologies[11]. A typical CKD consequence brought on by hypocalcemia, hyperphosphatemia, and low vitamin D levels is secondary hyperparathyroidism. Usually, these raised PTH levels are observed in conjunction with elevated FGF-23 levels[12,13]. Also, it was discovered that PTH infusion can raise FGF-23 levels in males in good health, showing that FGF-23 is elevated in those with hyperparathyroidism[14,15]. There is also evidence that calcium can increase the expression of FGF-23 on its own[16]. Serum FGF-23 levels are high in CKD due to hyperphosphatemia, and phosphate binders and dietary phosphate restriction are being utilized to lower FGF-23 levels. When it comes to pediatric patients, intact FGF-23 concentrations may be a helpful diagnostic for the early detection of X-linked hypophosphatemia [17]. It's interesting to note that studies have shown that while calcium-free phosphate binders do reduce serum FGF-23 levels, calcium-containing phosphate binders do not[18,19]. However, there are currently no reliable biomarkers for differentiating patients with nephrotic syndrome (SSNS) and (SRNS), in addition to determining the likelihood of Frequent relapse, where prolonged steroid therapy or renal biopsy can still be relied upon[20]. Finding novel biomarkers that can accurately and swiftly diagnose these people is therefore critically needed. Therefore, the purpose of this study was to evaluate if FGF-23 may be used as a biomarker to determine the probability of frequent relapse in addition to distinguishing the SSNS from SRNS when treated with glucocorticosteroids (GCS) in children from Iraq.

Materials and Methods

This cross-sectional study was conducted between February 15, 2022, and August 20, 2022, including Iraqi children with idiopathic nephrotic syndrome whom age range of 2 and 14 were chosen from the Pediatric Nephrology Consultation Center at Children's Teaching Hospital - Baghdad Medical City-Baghdad City and Al-Batoul Teaching Hospital for Women and Children - Diyala City under the guidance of a specialized physician. There were a total number of 125 participants in this study, of which 85 patients who were already diagnosed with steroid-sensitive or steroid-resistant INS were divided into four groups: 50 children with (SSNS) were in the first group (20) in relapse and the second (30) in remission, while 35 patients had (SRNS) were divided into the third group (20) in the relapse phase and the fourth group (15) in the remission phase, while the control group included 40 healthy children who were matched in age and gender to the patients. Patients with active urinary tract infections, congenital nephrotic syndrome, and secondary nephrotic syndrome to systemic diseases such as lupus nephritis, viral infections, or diabetes were excluded. The children classified as steroid-sensitive were those who showed no proteinuria on early morning urine dipsticks (less than 1+) during the first four weeks of daily prednisolone medication (2 mg/kg/day or 60 mg/m2 and a maximum daily dose of 60 mg/day). To put it another way, the children in the steroid-resistant group were those who, after eight weeks of daily prednisolone or four to six weeks of daily prednisolone regimen (2 mg/kg/day or 60 mg/m2 and a maximum daily dose of 60 mg/day) followed by another four to six weeks of alternate day prednisolone regimen (1.5 mg/kg/day or 40 mg/m2 and a maximum daily dose of 50 mg/day), did not achieve remission (<1+ proteinuria on early morning urine dipstick). Relapse: Heavy proteinuria is defined as a corresponding to 3+ or 4+ (protein excretion = 300 mg/dL or 2.0-5.0 mg/hour) by urine dipstick test for 3 consecutive days after remission, edema, hypoalbuminemia (less than 2.5 g per dL), and hyperlipidemia. Frequent relapse: is defined as (2 relapses within 6 months or ≥4 relapses within 12 months). Blood samples were drawn from the cubital vein after an overnight fast. Samples were clotted for 30 minutes, and centrifuged at room temperature for 10 minutes, to obtain serum. Urine samples are also taken from patients to examine total protein using urine dipsticks Serum concentrations of FGF-23 were assessed by ELISA using kits manufactured by Sunlong Biotech Co., Ltd, China (FGF-23: reagent kit SL2010Hu) and Klotho was assessed by ELISA using kits manufactured by Bioassay Technology Laboratory, China (Klotho: reagent kit E2781Hu). Measurements were taken according to the instructions provided by the manufacturer. The PTH hormone was also measured using the (Roche/Hitachi Cobas e 411 device), which uses the electrochemiluminescence immunoassay “ECLIA” technique, as for Serum Albumin, Cholesterol, and phosphorous, were measured using a device (Roche/Hitachi Cobas c 311).

Statistical analysis

The obtained data were analyzed using the statistical package of social science SPSS software (version 23.0). Percentages and absolute values are

used to display categorical data. Minimum and maximum values, along with the mean and standard deviation (SD), are displayed for continuous data. The Kolmogorov-Smirnov test was used to assess the normality of the data. One-way Analysis Of Variance (ANOVA) was done to compare the mean differences between groups. The differences between two selected groups in multiple pairwise comparisons using post-hoc tests (Games-Howell in equal variances assumed and Bonferroni for equal variances not assumed) were presented as p-values. The chi-square test was used for categorical variables. P values < 0.05 were considered statistically significant. To ascertain the FGF-23 level's discriminating potential in differentiating SSNS patients from SRNS patients and to determine the probability of Frequent relapse, the receiver operator characteristics (ROC) curve was examined. Pearson's correlation test was used to determine the relationship between the two parameters.

Results

Demographic information (Table 1) shows no significant differences between the groups under study. Regarding Age and Weight, there were no significant differences between SSNS patients in the relapse and remission groups, compared to the control group (P=1.000 for all pairwise comparisons) Also, there is no difference when comparing SRNS patients in the relapse and remission groups with the control group (p=0.400, p=0.994, respectively). Also, regarding Height, there were no statistical differences in SSNS and SRNS patients in the relapse and remission groups compared to the control group (P=1.000 for all pairwise comparisons). For BMI in SSNS patients in the relapse and remission groups compared to the control group (P= 1.000 for all pairwise comparisons) and BMI for SRNS in the relapse and remission groups compared to the control group (p=1.000, p=0.112, respectively).

Table 1. Demographic characteristics of the studied groups.

Parameters	SSNS (n=50)		SRNS (n=35)		Control (40)	P Value
	Relapse (n=20)	Remission (n=30)	Relapse (n=20)	Remission (n=15)		
Age (years) Mean±SD Min-Max	7.60±3.95 (2-14)	7.66±3.75 (2-14)	9.55±3.03 (4-14)	8.26±2.37 (5-13)	7.70±3.77 (2-14)	0.217[a]
Weight (Kg) Mean±SD Min-Max	29.28±11.06 (13.60-47.20)	29.46±10.51 (13.60-47.20)	34.74±8.49 (19.20-47.20)	31.14±6.64 (22.00-44.40)	29.56±10.55 (13.60-47.20)	0.217[a]
Height (Cm) Mean±SD Min-Max	121.20±22.39 (86.00-153.00)	121.03±20.52 (81.00-155.00)	130.40±14.50 (101.00-155.00)	126.40±10.09 (107.00-140.00)	122.50±20.24 (88.00-155.00)	0.360[a]
BMI (Kg/m2) Mean±SD Min-Max	19.14±1.01 (17.56-21.27)	19.45±1.45 (17.43-23.04)	20.10±1.63 (17.85-22.68)	19.31±2.09 (16.33-22.65)	19.00±1.15 (16.77-21.57)	0.310[a]
Gender [n(%)] Male Female	12(60.0) 8(40.0)	16(53.3) 14(46.7)	13(65.0) 7(35.0)	9(60.0) 6(40.0)	23(57.5) 17(42.5)	0.984[b]

a: One Way Analysis of Variance (ANOVA) test was used to determine whether the mean difference was significant at the 0.05 level of analysis.

b: Chi-square test was used.

SSNS: Steroid Sensitized Nephrotic Syndrome, SRNS: Steroid Resistant Nephrotic Syndrome.BMI: Body mass index.

There were highly significant differences among the studied groups Regarding laboratory data of the studied groups (Table 2). Subjects with INS had significantly higher serum Cholesterol, phosphorus, and PTH levels and lower serum albumin values compared to controls (p<0.05). The albumin levels of patients in the relapse phase decreased more than those in the remission phase (p < 0.0001 for all pairwise comparisons). The levels of cholesterol, phosphate, and PTH were higher in the relapse phase than in the remission phase in SSNS and SRNS patients (p<0.001 for pairwise comparisons). There were no statistical differences between SSNS and SRNS patients in the relapse phase in serum albumin, cholesterol, phosphorus, and PTH (p= 0.995, p= 0.372, p= 0.225, and p= 0.998 respectively).

Table 2. Biochemical characteristics of the of the participants.

Biochemical characteristics	SSNS (n=50)		SRNS (n=35)		Control (40)	P Value
	Relapse (n=20)	Remission (n=30)	Relapse (n=20)	Remission (n=15)		
Serum Albumin (g/dL) Mean±SD Min-Max	2.64±0.47* (1.98-3.70)	3.67±0.40* (3.04-4.50)	2.74±0.48* (1.98-3.70)	3.79±0.39* (2.90-4.50)	4.69±0.50 (3.50-5.20)	<0.001
Cholesterol (mg/dL) Mean±SD Min-Max	304.26±39.73* (254.10-366.30)	242.75±46.16* (171.50-325.70)	329.42±35.80* (260.80-380.60)	227.56±39.90* (170.20-300.00)	172.52±7.57 (159.80-188.30)	<0.001
Phosphorus (inorganic) Mean±SD Min-Max	5.92±0.63* (4.51-6.84)	4.48±0.66 (3.01-5.98)	5.55±0.78* (4.10-6.75)	4.86±1.00 (3.11-6.88)	4.26±0.56 (3.39-5.42)	<0.001
PTH (pg/ml) Mean±SD Range	113.95±6.74* (101.70-130.40)	92.45±4.35* (84.70-103.20)	112.03±15.20* (93.10-133.20)	94.72±5.80* (88.40-108.90)	83.75±2.34 (80.10-88.50)	<0.001

One Way Analysis of Variance (ANOVA) test was used to determine whether the mean difference was significant at the 0.05 level of analysis.

* Indicates that there is a significant difference with the control group.

Table 3 shows that the increase in FGF-23 was significant in all patients, whether in the relapse or remission group, compared to the control group ($P < 0.0001$), but the increase was higher in relapse, especially in SRNS patients, as there was a significant difference when comparing the relapse group of SRNS patients with The relapse group for SSNS patients ($P < 0.0001$), and the same applies when comparing the remission groups with each other, where the increase tends to favor the SRNS group ($P < 0.001$). On the other hand, Klotho levels decreased in SSNS and SRNS patients, whether in relapse or remission, with a significant difference compared to controls ($P < 0.0001$ for all pairwise comparisons). However, there were no differences when comparing klotho levels in the relapse group of SSNS patients with the relapse group of SRNS patients ($P = 0.143$) and when comparing the remission groups with each other ($P = 1.000$).

Table 3. Levels of Fibroblast growth factor-23 and Klotho protein in the studied groups.

Parameters	SSNS (n=50)		SRNS (n=35)		Control (40)	P Value
	Relapse (n=20)	Remission (n=30)	Relapse (n=20)	Remission (n=15)		
FGF-23 (ng/L) Mean±SD Range	51.73±8.79 (35.71-66.81)	16.49±2.23 (12.19-19.98)	67.25±9.39 (48.51-82.39)	24.66±3.35 (20.02-29.86)	7.73±2.33 (4.04-11.45)	<0.0001
Klotho (pg/ml) Mean±SD Range	251.10±33.21 (194.04-307.72)	206.09±33.10 (128.85-269.92)	219.86±43.96 (153.07-284.67)	211.00±40.78 (162.82-278.80)	378.47±37.84 (297.29-461.97)	<0.0001

One Way Analysis of Variance (ANOVA) test was used to determine whether the mean difference was significant at the 0.05 level of analysis.

The receiver operator characteristic (ROC) curve was used to evaluate the ability of FGF-23 to discriminate between (INS) patients with frequent relapse. According to the results, FGF-23 level had excellent reliable power as an identifying parameter [area under the curve (AUC)=0.941, $p<0.0001$]. With a cut-off value of 16.055 ng/L, ROC curve analysis of FGF-23 levels also revealed a test sensitivity of 100.0% and specificity of 77.8% at an asymptotic 95% confidence interval (0.883-0.998) for distinguishing pediatric nephrotic syndrome patients with frequent relapse from those patients who do not relapse frequently (Figure 1).

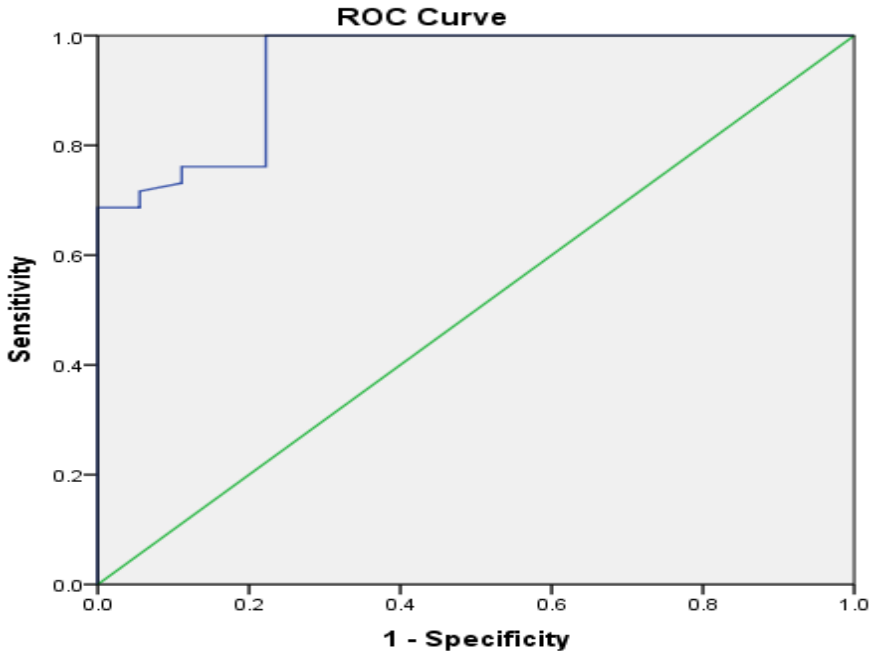

Figure 1. Receiver operator characteristic (ROC) curve analysis of FGF-23 to distinguish recurrent relapse status of patients

Also, The Receiver operator characteristic (ROC) curve was used to assess FGF-23's capacity to differentiate between children with SRNS and SSNS. According to the results, the FGF-23 level had a good dependable power as an identifying parameter [Area Under the Curve (AUC)=0.804, p<0.0001]. With a cutoff value of 20.00 ng/L, the ROC curve analysis of FGF-23 levels likewise revealed a test sensitivity of 54.2% and specificity of 90.0% at an asymptotic 95% confidence interval (0.712-0.896) to distinguish children with SRNS from those with SSNS (Figure 2).

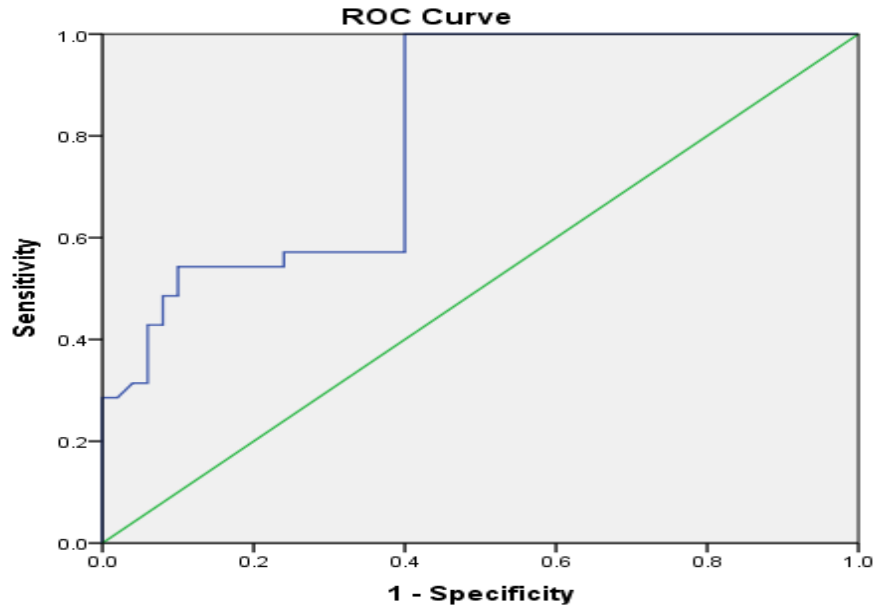

Figure 2. Receiver operator characteristic (ROC) curve analysis for FGF-23 to differentiate between (SSNS) and (SRNS) patients.

The analysis of the relationship between FGF-23 levels and albumin levels, showed a negative correlation (r = -0.675, p<0.0001). In contrast, the relationship between FGF-23 levels and klotho levels was positive, but very weak, closer to a negative relationship (r = 0.032, p = 0.772). On the other hand, a noteworthy positive connection (r = 0.672, p<0.0001) was seen between FGF-23 and cholesterol. Concerning parathyroid hormone and phosphorus, the correlation was positive (r = 0.516, p<0.0001, and r = 0.347, p=0.001, respectively) (Figure 3).

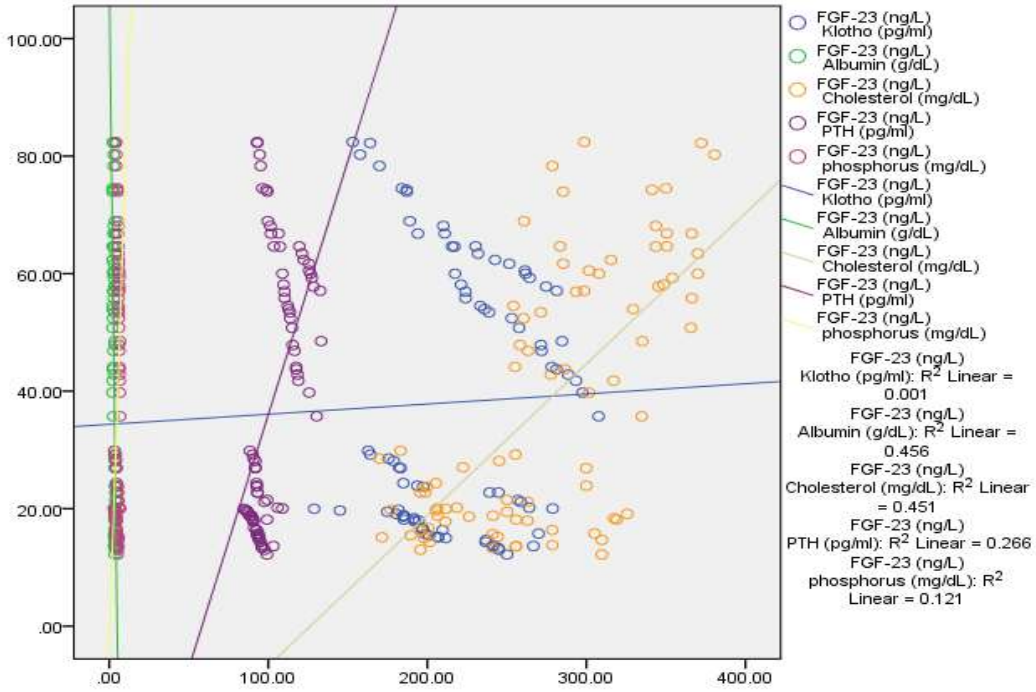

Figure 3. Correlation between klotho, albumin, parathyroid hormone, cholesterol and phosphorus, and FGF-23 level. FGF-23, fibroblast growth factor-23.

Discussion

One of the most prevalent primary kidney disorders nowadays is INS, and its progressive stages have the potential to lead to chronic kidney disease. The majority of INS patients respond well to steroid treatment, which improves their prognosis. According to the International Study of Kidney Disease in Children (ISKDC), Steroids are the recommended course of treatment. Steroid sensitivity is one of the side effects of drugs that are used to treat INS. Severe side effects from steroid treatment include hypertension, osteoporosis, growth retardation, and bone fractures like Nephropathic Cystinosis[21,22]. As there is currently no biomarker that can identify the kind of disease—SSNS or SRNS—Steroids are used as both a therapeutic and diagnostic intervention at the same time Histological examination by kidney biopsy is also used to determine the disease[23]. We conducted this study to test FGF-23 and see if it can be relied upon to determine the type of disease by comparing FGF-23 concentrations during the relapse and remission phases and also to determine the probability of Frequent relapse in these patients.

In this study, we demonstrated that the sociodemographic variables of age, sex, weight, height, and BMI did not significantly differ across the groups under investigation. In this study, we confirmed that there was a significant difference between SSNS and SRNS patients regarding serum FGF-23 concentrations compared to the healthy group ($P < 0.0001$), Also, FGF-23 levels were higher in SRNS patients compared to SSNS patients in both remission and relapse phases ($p < 0.0001$).

Our results are consistent with studies that have proven the role of FGF-23 in various kidney diseases. Pukajło-Marczyk et al. in Poland also identified a significant difference between NS patients and the healthy group and revealed that FGF-23 concentrations were higher in NS patients in relapse compared to patients in remission[24]. Significantly higher FGF-23 concentrations were confirmed in patients in whom the underlying cause of CKD was glomerulopathy. Ammar, Y. A. et al. found that circulating FGF-23 was associated with albuminuria and the development of CKD in patients[25]. In chronic kidney disease (CKD), fibroblast growth factor 23 (FGF23) has become a significant biomarker[26]. FGF-23 is acknowledged to be a reliable indicator of bone metabolic disorders brought on by chronic kidney disease[27]. Palupi-Baroto et al. studied plasma FGF-23 concentrations in children with chronic kidney disease and the aim was to determine the role of FGF23 as a biomarker in assessing cardiac changes in children with chronic kidney disease. The researchers concluded that FGF23 can be used as an early biomarker for detecting cardiac changes in pediatric CKD patients[28]. The results of our study also indicate a significant decrease in serum concentrations of klotho in all patient groups, whether in the case of SSNS or SRNS, compared to the control group, while there is no significant difference when comparing the SSNS and SRNS groups with each other. Klotho acts as a co-receptor for FGF-23 to perform its vital role on proximal tubular cells. Since albumin is also reabsorbed in both the proximal and distal nephrons[29], We thought it might also change

Klotho's expression. Decreased Klotho has been reported in early CKD categories decreased expression of Klotho in tubular epithelium beyond the loss of Klotho producing cells enhances resistance to fibroblast growth factor 23[30].

In both SSNS and SRNS patients, phosphate serum levels were higher regardless of elevated levels of FGF-23. We confirmed that serum phosphate concentration increased significantly in the relapse phase, in patients with SSNS, with a positive correlation between FGF-23 and serum phosphate concentration ($r = 0.347$, $P = 0.001$). There appears to be an indication of FGF-23 resistance in SSNS and SRNS patients, which is evidenced by observations such as a positive correlation of FGF-23 with serum phosphate concentration ($r= 0.347$, $P = 0.001$) as well as decreased biological activity of FGF-23 which may have a role in retention phosphate-induced proteinuria.Results of studies confirmed in nephrotic children and patients with CKD indicate that tubular handling of phosphates can be changed by proteinuria[31]. During glomerular proteinuria (relapse) serum phosphate concentration increases independently of GFR, as well as disturbances in thyroid and parathyroid hormones in renal children and patients with chronic kidney disease [32,33].

The results of our current study have demonstrated a relationship between albuminuria and elevated serum phosphate concentration despite elevated serum levels of FGF-23 and PTH in patients with nephrotic syndrome. We have found that PTH concentrations in the serum of Children with nephrotic syndrome, whether SSNS or SRNS, similar to FGF-23 concentrations, increased in the relapse phase. These results are consistent with those of Tomo, et al. [34] who found that serum albumin, serum phosphate, and PTH significantly differed between the nephrotic group and the healthy group. Contrary to the findings of Abd Alridha et al., who reported that blood albumin and cholesterol were lower in SSNS patients than in SRNS patients[35], we did not observe a significant difference in serum albumin or total cholesterol between SRNS and SSNS. On the other hand, Dewang Zeng et al., found that FGF-23 was positively correlated with PTH and calcium, but there were no statistical correlation with phosphate[36]. While Imran Hussain et al., found no statistically significant correlation to suggest an effect of FGF-23 on these parameters[37]. After all, the current study has some limitations related to the limited number of participants, which limits the generalizability of the results. There is also the variation in the disease duration and thus the length of treatment that the patients received. In addition, we could not follow the same patient in the relapse and remission phases due to the variation in the time required to reach partial or complete remission.

Conclusion

We can conclude that High levels of FGF-23 in children with INS are more associated with the occurrence of relapse as well as the progression of the disease to SRNS, Therefore, monitoring FGF-23 levels in INS patients is very necessary to know the extent of the disease's progression. according to the ROC test, FGF-23 could be a potential biomarker to identify patients with recurrent relapses at a cut-off value of (16.055 ng/L). Also, but to a lesser extent, FGF-23 may be a biomarker to differentiate patients with SSNS from patients with SRNS at a cut-off value of (20.00 ng/L). The significance of these observations requires further research on a larger group of patients.

Conflicts of Interest

There are no conflicts of interest.

Funding

Nil.

Ethics Statements

Approval was obtained from the local ethical committee in the Medical City-Baghdad/Children Welfare Teaching Hospital approved the project Also, the Scientific Research Committee in the Diyala Health Department agreed to conduct this research. Before formal agreement was gained, the parents or guardians of the children were informed about the study's goal and procedures. Oral consent was sought from the child before the commencement of the evaluations.

Author Contribution

The authors confirm their contribution to the paper as follows: study conception and design, interpretation of results: Nawal M.J. Al-Shammaa; data collection, analysis, and draft manuscript preparation: Ahmed Hatem Alwan. All authors reviewed the results and approved the final version of the manuscript.

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تقييم عامل نمو الخلايا الليفية-٢٣ وبروتين كلوثو لدى الأطفال المصابين بالمتلازمة الكلوية الحساسة للستيرويد والمتلازمة الكلوية المقاومة للستيرويد

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الخلاصة

المتلازمة الكلوية مجهولة السبب هي مرض شائع يصيب كلى الأطفال وتحدث بسبب خلل محدد في الكبيبات مما يؤدي إلى تسرب البروتين إلى البول بكميات كبيرة. يعد عامل نمو الخلايا الليفية -٢٣ (إف جي إف -٢٣)، الذي تنتجه العظام، ضروريًا للتحكم في استقلاب ١، ٢٥ -ثنائي هيدروكسي فيتامين د والفوسفات، ولكنه يتطلب أيضًا مستقبله المساعد كلوثو لأداء وظيفته. لذلك، كان الغرض من هذه الدراسة هو تقييم ما إذا كان يمكن استخدام (إف جي إف -٢٣) كمؤشر حيوي لتحديد احتمالية الانتكاس المتكرر وكذلك للتمييز بين المتلازمة الكلوية الحساسة للستيرويد والمتلازمة الكلوية المقاومة للستيرويد. لمرضى يعالجون بالجلوكوكورتيكوستيرويدات. في هذه الدراسة المقطعية، تم تقسيم ٨٥ مريضًا يعانون من المتلازمة الكلوية مجهولة السبب إلى أربع مجموعات: من بين (٥٠) طفلًا مشمولين في هذه الدراسة مصابين بالمتلازمة الكلوية الحساسة للستيرويد تم تجميعهم في المجموعة الأولى (٢٠) في حالة الانتكاس والثانية (٣٠) في المغفرة بالإضافة إلى ٣٥ طفلاً مصاباً بـالمتلازمة الكلوية المقاومة للستيرويد تم تقسيمهم إلى: المجموعة الثالثة المكونة من (٢٠) طفلاً في مرحلة الانتكاس والمجموعة الرابعة المكونة من (١٥) طفلاً في مرحلة المغفرة، بينما ضمت المجموعة الضابطة ٤٠ طفلاً أصحاء. تم قياس مستويات (إف جي إف -٢٣) ومستقبله المساعد كلوثو في هؤلاء المرضى باستخدام تقنية الإليزا. كشفت نتائجنا أن مستويات مصل (إف جي إف -٢٣) كانت مرتفعة بشكل ملحوظ في مرضى المتلازمة الكلوية الحساسة للستيرويد بمتوسط (٥١.٧٣ نانوغرام / لتر) في الانتكاس و (١٦.٤٩ نانوغرام / لتر) في مغفرة، بينما في المجموعات المقاومة للستيرويد (٦٧.٢٥ نانوغرام / لتر) في الانتكاس و (٢٤.٦٦ نانوغرام / لتر) في مغفرة، مقارنة مع المجموعة الضابطة بمتوسط ٧.٧٣ نانوغرام / لتر ($p < ٠.٠٠٠١$). وفي الوقت نفسه، انخفضت تركيزات كلوثو لجميع مجموعات المرضى مقارنة بالمجموعة الضابطة. ومن ثم، فإن مستوى المصل (إف جي إف -٢٣) هو علامة حيوية محتملة لتحديد المرضى الذين يعانون من الانتكاسات المتكررة عند قيمة قطع (١٦.٠٥٥ نانوغرام / لتر). بينما كانت قدرته اقل في التمييز بين مرضى المتلازمة الكلوية الحساسة والمقاومة للستيرويد عند قيمة قطعية قدرها (٢٠.٠٠ نانوغرام/لتر).

الكلمات المفتاحية:. عامل نمو الخلايا الليفية -٢٣، كلوثو، المتلازمة الكلوية مجهولة السبب.