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Clinical Exploration of Medicines used in the Patient with Nephrotic Disorders and its Consequence on Endocrine Function

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Abstract

The massive losses of albumin and hormone-binding proteins are responsible for metabolic derangements with endocrine abnormalities in nephrotic patients. A Population-based longitudinal study in north Indian hospitals for risk factor of cardiac remodeling appropriate to the prescription of anti-nephrotic drugs on 87 nephrotic patients were observed during the clinical survey. The kidney function test, lipid profile and thyroid profile with vitamin-D has been recommended for all patients. The laboratory values such as SGOP (25.80±10.86 IU), SGPT (22.72±13.50 IU) and GGTP (57.58±89.27 IU) were merely elevated in comparison to normal values and confirms the disturbance in liver function. Serum Protein (6.87±7.47 gm/dl), Serum Albumin (3.78±1.11 gm/dl), Serum Globulin (3.34±0.96 gm/dl) and 24 Hour Protein (2950.30±1856.94 mg) confirmed the demolition in the liver enzyme. The elevated levels of urinary profile confirm that all patients have been suffering from kidney disorders, which influence the cardiac function because of the accumulation of creatinine and urinary protein in the body. The deficiency of vitamin D plays a vital role in cardiac remodeling, which is maintained by the normal and routine function of the kidney.

Keywords: *Nephrotic disorder, Kidney, Creatinine, Vitamin D, Albumin, Endocrine.*

Introduction

The nephrotic syndrome is a nonspecific urinary organ disorder characterized by three signs of diseases i.e., massive proteinuria (>40 mg/m^2/hr), hypoalbuminemia (<2.5 g/dL), hyperlipidemia (3 g/1.73 m^2 body surface area per day) and in most cases the generalized edema begins with the face [1,2]. Principally, loss of protein through the excretory organ (proteinuria) leading to low protein levels within the blood (hypoalbuminemia), which causes retention of water into soft tissues (edema) that confirms the diagnosis of nephrosis. Additionally, hyponatremia occurs with a low fractional sodium excretion. Terribly hypoalbuminemia even may cause a spread of secondary issues, i.e., water within the abdominal cavity (ascites), in the region of the heart or lung (pericardial effusion, pleural effusion), high cholesterol (hyperlipidemia), loss of proteins that regulating coagulation [3].

The hyper albuminuria occurs due to a rise in a porosity of the "filtering membrane" of the urinary organ that unremarkably separates the blood from the urinary compartment within the Bowman's capsule [4]. This is composed of the capillary walls of the glomerulus wrapped by extremely specialized cells known as podocytes. In contrast, the patient suffering from nephrotic syndrome, the RBCs pass through the pores and inflicting haematuria [5].

Endocrine Irregularities

The associated urinary losses of albumin and hormone-binding proteins are responsible for many of the metabolic derangements with endocrine abnormalities in nephrotic patients [6]. The thyroid function tests of nephrotic patient reveal variable

results typically depend on the losses of protein in the urine. The other factors that frequently observed with the nephrotic syndrome, i.e., hypoalbuminemia, increased serum levels of free fatty acid are also affecting normal thyroid function [7-9].

The urinary losses of thyroxine (T4)-binding globulin (TBG) and other thyroid hormone-binding proteins (transthyretin and albumin) with T4 bounding resultant in the low level of total T4 concentrations observed in around 50% of nephrotic patients with a relatively normal glomerular filtration rate (GFR) [10]. Serum triiodothyronine (T3) concentrations may also be low and be causing decreased binding. There is often a good correlation between the serum concentration of T4, T3, and albumin whereas serum reverse T3 (rT3) concentrations are also reported as low [11]. The abnormalities in thyroid function are often more severe in the patient with renal failure or nephrotic disorder and the serum TSH level must be measured in hypothyroidism patient [12].

The administration of glucocorticoids often controls the nephrotic condition but may cause a small reduction in TSH secretion by inhibiting the peripheral conversion of T4 to T3. The net effect may be persistently low serum T3 and basal serum TSH concentrations, and a rise in serum rT3 concentrations [13]. Thus, the serum free T4 concentrations may be the best marker of thyroid status. Patients with low serum free T4 concentrations probably should be treated as if they were hypothyroid [14].

The secondary causes of nephrotic syndrome are associated with autoimmune thyroid disease, for example, the membranous nephropathy has been associated with both autoimmune thyroiditis (Hashimoto's disease) and Grave's disease [15,16]. Antithyroid antibodies have been reported in the glomerular immune deposits in Grave's disease [17]. Whereas thyroidectomy was associated with the disappearance of antithyroid antibodies, reduction of proteinuria and stabilization of GFR. Conversely, treatment of patients suffering from Grave's disease with radioactive iodine had reported as the appearance of membranous nephropathy and proliferative glomerulonephritis [18,19].

Abnormal endocrine function in adolescent boys treated long-term for steroid-sensitive nephrotic syndrome corresponded with the clinical picture of delayed onset of puberty, which accounted for severe growth retardation in a substantial proportion of subjects [20].

Cardiovascular Complications

Globally it was observed that the increased risk of cardiovascular disease exists in patients with NS because of hyperlipidemia, increased thrombogenesis, and endothelial dysfunction [21]. Hypercholesterolemia is strongly associated with severity of hypoalbuminemia, and persistent proteinuria or renal insufficiency may also contribute to cardiovascular disease [22].

Research Methodology

Patients Profile

Selection Criteria of Patients

A Population-based longitudinal study in north Indian hospitals for risk factor of cardiac remodeling due to the prescription of anti-nephrotic drugs were observed through the selection of about 87 patients suffering from kidney, heart and any other diseases at the age of more than 40 years [23,24]. The selection of patients' typically based on inclusion criteria and exclusion criteria as mentioned below;

Inclusion Criteria

Male and female patients with the complication of kidney and heart disease was select for the study.

Exclusion Criteria

Patient of either sex with any other associated diseases were excluded from the study [25].

Clinical Surveillance of Medicine

All the patients were randomly divided into groups and subunits according to complications of disease and treatment medications allowance [26].

The sample size was calculated by using the following equation.

Sample size (n) = $Nz^2Pq / L^2 (N-1) + z^2Pq$

Where; n=Sample size, P=Prevalence rate, q=100-P, l=Allow error, z=Standard normal distribution, N=total study population

Laboratory Parameters

kidney function test, lipid profile and thyroid profile with vitamin-D has been recommended for all patients. Elevated levels of all reported parameters were compared with each other as well as with normal baseline of the population [27].

Design of the Clinical Assessment

Types of Studies

RCTs and quasi-RCTs (in which allocation to treatment was obtained by alternation, use of alternate medical records, date of birth or other predictable methods), in any lipid-lowering agents, doses, routes of administration and treatment duration of nephrotic patients were included for the clinical survey [28].

Types of Participants

Both adults and children suffering from nephrotic syndrome were included for this survey. Diagnosis of nephrotic syndrome in adults was based on proteinuria greater than 3.5g/24 h and low serum albumin (<30g/L). Diagnosis of nephrotic syndrome in children was defined as proteinuria greater than 50mg/kg/24 h and serum albumin at 2.0g/dL. We also included criteria that the investigated participants with nephrotic syndrome but without a definition for nephrotic syndrome. The study excluded participants with hepatic disease, muscle disease, diabetes mellitus, systemic lupus erythematosus, hypothyroidism, carcinoma, lymphoma or amyloidosis and also excluded participants with histories of familial dyslipidemia [29].

Types of Interventions

The following interventions were included as; any lipid-lowering agents compared with no drug or placebo, the duration of study not less than four weeks, and the intervention as well as naive patients that used routine therapy simultaneously. The investigator excluded the patients from the study only when administered anti-proteinuria agents into an intervention group of participants [30].

Types of Outcome Measures

Primary Outcomes

All-cause mortality, cardiovascular mortality, non-fatal myocardial infarction, stroke, total serum cholesterol, LDL, HDL, serum triglyceride, blood urea nitrogen (BUN) and serum creatinine (SCr) were included as primary outcomes and measured after undergoing lipid-lowering therapy for at least four weeks.

Secondary Outcomes

Urinary protein excretion (g/24 h), serum protein, serum apoA and apoB; elevated liver enzymes, creatinine phosphokinase (CPK), rhabdomyolysis were included as secondary outcomes and measured after undergoing lipid-lowering therapy for at least four weeks.

Data Collection and Analysis

Selection of Studies

The selection of study based on the investigation of lipid-lowering agents as an intervention and a prospectively organized group of participants with nephrotic syndrome. The disagreement points during the selection of the study were resolved by the healthy discussion [31].

Data Analysis

Available data were summarized where sufficient clinical and methodological homogeneity was established. Statistical analysis was performed according to the statistical guidelines referenced in the Cochrane handbook for interventions [32]. Final it was planned to pool the data using the random-effects model and to apply the fixed-effect model to ensure robustness of the model selection and susceptibility to outliers [33].

Result and Discussion

The clinical survey on nephrotic patients have been accomplished of total 87 patients from Indraprastha Apollo Hospitals, Apollo Hospital, Delhi, GSG Hospital, RK Pathology and Clinic New Delhi, the detailed result of this survey are given as follow;

Selection of Patients

The details of patients profile with the medical history of all patients included in this survey are given in table 1. Total of 60 male patients and 27 female patients were preferred for this survey from different hospitals and clinics at New Delhi. The preferred patients having the average age of 51.20±13.53 years and the average weight of 68.44±7.30 kg. The average height of all patients have been measured around 167.93±7.11 cm, these patients have fallen in all ABO blood group types and the renal GFR were recorded as 78.59±12.61 ml/min during diagnosis. SAF, RAR, Nankivell, CKD, DN, Obstructive Uropathy, Hyperuricemia, Gout nephropathy, Uremia were diagnosed from all patients.

Table 1. *Details of patients profile with diagnosis and blood group affirmation*

Sr. No.	Age (Year) Mean±SD	Sex (M/F)	Height (cm) Mean±SD	Weight (Kg) Mean±SD	Blood Group (O,A,B,AB)	Renal Diagnosis GFR (ml/min)
1.	51.20±13.53	60 Male 27 Female	167.93±07.11	68.44±07.30	O^{+Ve} A^{+Ve} B^{+Ve} AB^{+Ve}	78.59±12.61
2.	Renal Diagnosis		SAF, RAR, Nankivell, CKD, DN, Obstructive Uropathy, Hyperuricemia, Gout nephropathy, Uremia			
3.	Comorbid Diagnosis		DM, EDS, Hypertension, Secondary Hyperparathyroidism, Anaemia, Hyperuricemia, Coronary artery disease			

Data were expressed as mean±SD for patients Age, Height, and Weight, while the Renal Diagnosis GFR was expressed as ml/min; (n=87); Where SAF-Stable allograft function, RAR-Renal allograft recipient, CKD-Chronic kidney disease, DN-Diabetic nephropathy, DM-Diabetes mellitus, EDS-Ehlers-Danlos syndrome.

Prescribed Medications

The treatment medication of all patients used during the medical therapy to resolve the worse condition and maintain normal function of the patients. The medicines used in the treatment of nephropathy producing somewhere adverse effects which were disappeared until the end of therapy, but influences the biological functions after prolonged administration.

All the medicine used in the treatment of nephrotic disorders was allopathic drugs. It is well reported that the allopathic medicine producing side effect when used for a long time with other concomitant medicines. The combination therapy of medicines generally producing drug interaction when simultaneously administered in the human body and has several factors for producing unwanted effect after interacting with the biological system.

Administration of numerous medicine adversely inducing the workload on vital organs such as; kidney, liver, heart, pancreas, etc. due to this the normal physiology of human body become critical and disturbed their routine function to meat good survival of life. The normal function of the heart is totally depending on normal kidney function. When anyone fails to achieve their normal function, it produces the elevation of a biological system and several biochemical parameters.

Laboratory Diagnosis

The complete blood profile of all patients was observed from laboratory report, this observation confirms that all the reported parameter has elevated in comparison to normal values. These elevated parameters confirm that all patients have been suffering from diabetes and kidney disorders, which is highly required for critical monitoring and initiation of early treatment (Table 2). The goals for the treatment were differed as per the patient condition and fluctuated laboratory parameters.

Table 2. *Laboratory parameters (serum profile) of all patients*

Sr. No.	Parameter	Normal Values	Observed Values
1.	Hb(gm/dl)	13–17 (Male) 11–15 (Female)	10.34±2.52
2.	Neutrophil	45–75	69.31±15.30
3.	Lymphocyte	20–45	21.02±11.75
4.	Monocyte	2–10	4.95±2.32
5.	Eosinophil	1–6	2.55±1.87
6.	TLC (cm^3)	400–10000	8792.09±19049.16
7.	Platelet Count (cm^3)	14000–44000	195296.20±117200.91
8.	ESR (mm/hrs)	0–15	48.33±36.92
9.	Serum Urea (mg/dl)	10–50	97.24±76.84
10.	Serum Creatinin(mg/dl)	0.5–1.3	5.22±5.61
11.	Serum Sodium (meq/dt)	130–145	143.52±16.17
12.	Serum Potassium (meq/dt)	3.5–5.0	4.63±1.47
13.	Serum Calcium (mg/dl)	8.4–10.2	7.37±1.99
14.	Serum Phosphorus (mg/dl)	2.7–4.5	4.42±1.84
15.	Serum Alk Phosphate (IU)	39–117	129.40±70.45

All the data expressed as Mean±SD and the total number of patients (n=87), Normal values of all parameters fluctuate from different laboratories

Liver Function Test

The Liver function test of preferred patients for nephropathy was reported in table 3. The values of these tests i.e. SGOP (25.80±10.86 IU), SGPT (22.72±13.50 IU) and GGTP (57.58±89.27 IU) were merely elevated in comparison to normal values and confirms the disturbance in liver function. Serum Protein (6.87±7.47 gm/dl), Serum Albumin (3.78±1.11 gm/dl), Serum Globulin (3.34±0.96 gm/dl) and 24 Hour Protein (2950.30±1856.94 mg) also confirmed the demolition in the liver enzyme.

Table 3. *Liver function test of preferred patients for nephropathy*

Sr. No.	Parameter	Normal Values	Observed Values
1.	SGOT (IU)	5–10	25.80±10.86
2.	SGPT (IU)	5–40	22.72±13.50
3.	GGTP (IU)	10–50	57.58±89.27
4.	Serum Protein (gm/dl)	6.6–8.7	6.87±7.47
5.	Serum Albumin (gm/dl)	3.5–5.0	3.78±1.11
6.	Serum Globulin (gm/dl)	2.8–4.5	3.34±0.96
7.	24 Hour Protein (mg)	10–140	2950.30±1856.94

All the data expressed as Mean±SD and the total number of patients (n=87), Normal values of all parameters fluctuate from different laboratories

Complete Blood Profile

The blood cholesterol test of all patients was observed from laboratory report, this observation confirms that all the reported cholesterol levels have been elevated in comparison to normal values (Table 4). The elevated levels of cholesterol confirm that all patients have been suffering from somewhat hypertension and kidney disorders, which is required regular monitoring and initiation of early treatment therapy. It is reported that the normal function of the heart entirely depends on normal kidney function. When anyone fails to achieve their normal function, it produces the elevation of a biological system and all biochemical parameters. The goals for the treatment were differed as per the patient condition and fluctuated laboratory parameters. Some patients required firstly manage heart disease and some patients need to first manage kidney function for normal filtrations of blood.

Table 4. *Cholesterol test with other clinical parameters of all patients*

Sr. No.	Parameter	Normal Values	Observed Values
1.	Serum Cholesterol (mg/dl)	200–239	141.98±52.25
2.	Serum Triglycerides (mg/dl)	45–150	96.75±59.30
3.	Serum VLDL (mg/dl)	2–30	34.15±24.17
4.	Serum HDL (mg/dl)	40–60	69.44±55.86
5.	Serum LDL (mg/dl)	100–130	78.22±38.24
6.	HBA1C (percent)	5.7–6.4	4.87±1.63
7.	Tacrolimus Levels (ng/ml)	5.0–15.0	6.44±3.52

All the data expressed as Mean±SD and the total number of patients (n=87), Normal values of all parameters fluctuate from different laboratories

Clinical Parameters for Trace Elements

Test report of trace element with other clinical parameters of all patients were observed from laboratory test report which reviles that serum iron (84.96±36.54 µg/dl), serum ferritin (182.69±163.99 ng/ml), TIBC (203.49±66.60 µg/dl), transferrin saturation (47.76±23.39 %), PTH (127.36±114.21 pg/ml) and vitamin D (48.49±22.98 ng/ml). These elevated parameters (Table 5) confirm that patients have been suffering from cardiac disturbance, diabetes and kidney disorders, which is extremely required for critical monitoring and initiation of early treatment therapy. The deficiency of vitamin D plays a vital role in cardiac remodeling, which is maintained by the normal and routine function of the kidney.

Table 5. *Test report of trace element with other clinical parameters of all patients*

Sr. No.	Parameter	Normal Values	Observed Values
1.	Serum Iron (µg/dl)	55–160 (Male) 40–155 (Female)	84.96 ± 36.54
2.	Serum Ferritin (ng/ml)	30–350 (Male) 15–300 (Female)	182.69 ± 163.99
3.	TIBC (µg/dl)	240–450	203.49 ± 66.60
4.	Transferrin saturation (%)	15–50	47.76 ± 23.39
5.	PTH (pg/ml)	10–65	127.36 ± 114.21
6.	Vit. D (ng/ml)	20–50	48.49 ± 22.98

All the data expressed as Mean±SD and the total number of patients (n=87), Normal values of all parameters fluctuate from different laboratories

Biochemical Parameters

The urinary profile (biochemical parameters) of all patients were observed from laboratory test report, this observation confirms that the reported biochemical parameters have been elevated in comparison to normal values (Table 6). These elevated levels of urinary profile confirm that all patients have been suffering from kidney disorders, which influence the cardiac function because of the accumulation of creatinine and urinary protein in the body. This is required critical monitoring and initiation of early treatment therapy to avoid the cardiac dysfunction.

Table 6. *Biochemical (urinary profile) parameters of all patients*

Sr. No.	Parameter	Normal Values	Observed Values
1.	Specific Gravity	1.002–1.030	1.07±0.14
2.	Urinary Protein (mg/dl)	0–20	1.20±0.77
3.	Pus Cells in Urine (p.v.f.)	0–4	2.91±1.78
4.	C.C. Cockcroft & Gault (ml min/1.73m2)	100–130	67.04±62.12
5.	C.C. MDRD (ml/min/1.73m2)	40–60	57.47±25.27
6.	Red Blood Cells	Occult	Nil/Occult
7.	Sugar in urine	Occult	Nil

All the data express as Mean±SD and the total number of patients (n=87), Normal values of all parameters fluctuate from different laboratories, C.C.=Creatinine Clearance (ml/min/1.73m^2)

Administration of numerous medicine adversely affecting the workload of vital organs such as; kidney, liver, heart, pancreas, etc. due to this the normal physiology of human body become critical and disturbed their routine function to meat good survival of life. The normal function of the heart is totally depending on normal kidney function. When anyone fails to achieve their normal function, it produces the elevation of a biological system and all biochemical parameters.

Discussion

The treatment goals were observed as per the patient condition and abnormal laboratory parameters. Some patients needed immediate treatments to manage heart disorders where few patients ought to manage urinary function for essential filtrations of blood to support the heart for their normal functioning.

The present clinical survey ascertained that the heart could be a major target of thyroid hormones and modification in the levels were required to test for the ordinary heart functions. Furthermore, a very little thyroid hormone as a consequence of an underactive thyroid (hypothyroidism) causes very slow heartbeat on an irregular basis and flutter with missing or extra heartbeats. As a consequence severe bradycardia could develop that escape organs and tissues without enough oxygen and nutrients lead to cardiac arrest. It may also cause a change in blood pressure because high blood pressure has widened the consequence of developing atherosclerosis that associated with a risk of heart attack and stroke.

Hypothyroidism may cause raise cholesterol level in the blood and calcification, so-called plaque, to develop inpatient arteries and make them stiff. All these effects increase the risk for heart attack, heart failure, and atherosclerosis.

In addition, a lot of thyroid hormone as a consequence of an overactive thyroid (hyperthyroidism) causes chest pain and palpitations that are not revealed by a heart check-up and the developed tachycardia may lead to the arrhythmia that implies the danger of heart attack or death. Hyperthyroidism may cause the rise in blood pressure subsequently called wide pulse pressure can enlarge with elevated systolic reading and normal diastolic reading. It is an important risk factor and predictor of mortality from heart disease, especially from atherosclerosis.

In addition to currently available treatments, a variety of novel therapies are undergoing clinical development for the prevention and treatment of kidney complications. As we can expect from the common pathology of diabetic uropathy and myocardiopathy, these new ways have the potential to supply new therapeutic choices within the management of each nephropathy and failure in polygenic disorder.

Among the foremost advanced in clinical development that agents modulate advanced glycation end products (AGE) and the activity of Protein Kinase C (PKC). The AGE formation resulting from a series of non-enzymatic reactions during which sugar derivatives covalently bind to proteins, forming irreversible cross-links that may accumulate in long-lived proteins such as collagen.

The accumulation of AGE within tissues leads to alterations in structure and function, with experimental evidence implicating them in the pathogenesis of diabetic complications, including those of the kidney and the heart. The strategies to attenuate the pathogenetic influence of AGE include prevention of AGE formation, blockade of AGE receptors, and breakers of AGE-protein cross-links.

PKC is a ubiquitously expressed as serine-threonine kinase transducing a wide range of cell-signaling process catalyzed by substrate- specific phosphorylation. It is typically relevance to cardiac and renal disease includes PKC-mediated increases in TGF-β and matrix-protein expression. It may also play a critical role in the activation of mitogen-activated protein kinase, and phenotypic changes in endothelial and smooth muscle cells.

Currently, the PKC inhibitor has been reported as most extensively in renal disease i.e., ruboxistaurin, a specific inhibitor of the PKC-β isoforms. The pre-clinical studies reported the mechanism of ruboxistaurin as not only to reduce TGF-β and collagen expression but also to attenuate mesangial expansion and albuminuria with evidence of renoprotection despite the presence of continuing hyperglycemia and hypertension.

The essential protein regulates the expression of antioxidant proteins to protect against oxidative damage triggered by injury and inflammation as a pivotal mediator for the antioxidant defense system. It may also play a critical role in preventing diabetes-induced oxidative stress, inflammation, and dysfunction of vital organs.

Conclusion

The basic problems relating to patients suffering from nephropathy and cardiopathy are merely resolving within the medical care center. In severe and advanced cases the health care professionals initially control hypertension, then reducing cholesterol level by intake of low dietary salt with restriction of phosphorus with potassium.

The primary goals of treatment are to relieve symptoms, prevent complications, and delay kidney damage during the management of nephrotic syndrome, must be treated the disorder that causing the following condition. First, keep blood pressure at normal or below 120/80mmHg to delay kidney damage. Angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) are the medicines most often used. ACE inhibitors may also help decrease the amount of protein lost in the urine. Patients may take corticosteroids and other drugs that suppress or quiet the immune system.

Treat high cholesterol to reduce the risk of heart and damage of blood vessels. A low-fat, low-cholesterol diet is usually not very helpful for people with nephrotic syndrome. The medicine usually statins that reduce cholesterol and triglycerides may be considered necessary. A low-salt diet may help with swelling in the hands and legs and diuretics also help to resolve this problem.

Low-protein diets may be helpful for improving the nephrotic syndrome. The health care provider may suggest eating a moderate-protein diet. Patients may need vitamin D supplements in long-term nephrotic syndrome when not responding to treatment. But sometimes it is not routinely recommended in patients with the nephrotic syndrome.

Pre-clinical studies scheduled the nephrotic syndrome have found that calcidiol absorption is probably sufficient at oral therapy of vitamin D and the similar findings have been also noted in humans [34]. The oral administration of calcidiol in nephrotic patients resulting in sustained normalization of the serum calcidiol concentrations. Patients with the nephrotic syndrome who develop chronic renal failure will often be at an increased risk for vitamin D-related bone disease due to the associated reduction in calcitriol synthesis [35].

Recommendations

Patients who have nephrotic syndrome but a relatively normal GFR may have a low serum level of total T4, T3, and reverse T3 (rT3) but normal serum level of free T4 and T3 concentrations, T3/T4 ratio, and thyrotropin (TSH) concentrations. Such patients are

usually not required thyroid hormone replacement therapy. If hypothyroidism is suspected clinically in such a patient, serum TSH should be measured.

The administration of glucocorticoids in nephrotic syndrome can cause low serum T3 and basal serum TSH concentrations and increased serum rT3 concentrations. The serum free T4 concentrations may be the best marker of thyroid status among such patients. Patients with low serum free T4 concentrations should be treated as if they were hypothyroid. Serum calcidiol and calcitriol concentrations may be reduced in patients with nephrotic syndrome, but the physiologically important serum free calcitriol concentration is usually normal. In hypoalbuminemia state, the hypocalcemia does not affect the physiologically important free (or ionized) calcium concentration.

In patients with the nephrotic syndrome, vitamin D replacement therapy is not routinely recommended. It may be beneficial in patients with persistent reductions in serum ionized calcium concentrations and/or abnormal bone histology; in such case oral therapy of vitamin D is probably sufficient. Although serum cortisol concentrations may be reduced due to loss of cortisol-binding globulin in the urine, serum free cortisol concentrations are normal, and symptomatic hypocortisolism does not occur in nephrotic patients.

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