Original Articles

LABORATORY ASSESSMENT OF THYROID FUNCTION IN PATIENTS WITH PROTEINURIA

Irena I. Gencheva-Angelova, Adelaida L. Ruseva, Juli I.Pastuhov

Department of Clinical Laboratory, Clinical Immunology and Allergology, MedicalUniversity – Pleven, Bulgaria

Corresponding Author:

Irena I. Gencheva-Angelova Department of Clinical Laboratory, Clinical Immunology and Allergology, MedicalUniversity– Pleven 1, St. Kliment Ohridski Str. Pleven, 5800 Bulgaria *e- mail: i_gencheva@dir.bg*

Received: October 05, 2017 Revision received: January 16, 2018 Accepted: February 27, 2018

Summary

Significant losses of functional proteins such as hormones and hormone-binding proteins are seen in patients suffering from proteinuria. Studies have reported loss of thyroid hormones and thyroxine-binding globulin in the urine. There is evidence that subclinical hypothyroidism is six times more common in patients with proteinuria than in healthy people. The parameters of the effect of proteinuria on thyroid function have not been fully studiedyet.We investigated 74 patients with qualitatively established proteinuria, of whom 34 men and 40 women, without diagnosed thyroid disease. The average age of the patients was 60.9 years. We tested 20 free controls for free thyroxine (FT4), thyroid stimulating hormone (TSH), creatinine and albumin in serum, and the quantity of urine protein. The mean results found for TSH were higher in the patients with proteinuria than in those of the controls (2.719 mU/l vs 1.78 mU/l). For FT4, the mean result in the patients with proteinuria was 17.04 pmol/l vs 16.39 pmol/l. in the controls. A correlation was sought between TSH and FT4 levels and all the laboratory parameters we tested. Patients with proteinuria had higher TSH levels, probably due to the loss of thyroid hormones in the urine. However, these losses cannot lead to clinically proven hypothyroidism.

Key words: proteinuria, TSH, FT4, hypothyroidism

Introduction

Proteinuria is a sign of potential kidney disease. Proteinuria, hypoalbuminemia, edema and hyperlipidemia characterize nephrotic syndrome. The mainprotein in serum and urinein patients with nephrotic syndrome is albumin, which is being lost in the urine [1, 2]. Hypoalbuminemia, as a consequence of these losses, cannot be fully set off by increased liver albumin synthesis. In proteinuria patients, apart from albumin, other proteins are also lost with the urine [3]. Among them are some hormones.

The loss of thyroid hormones and thyroxinebinding globulin (TBG) in the urine in patients suffering from proteinuria has been documented by several studies [4-8].The clinical significance of this fact has not been well studiedyet. The decrease of thyroid hormones could lead to low thyroid hormone levelsin patients suffering from nephrotic syndrome, unless the thyroid stimulating hormone (TSH) production increases [6, 8-10]. Moreover, loss of albumin and thyroxin binding globulin (TBG) may lead to reduction of the thyroid hormone binding capacity,which results in a reduction in total triiodothyronine (T3) and thyroxine (T4).

So far, there have been onlyfew studies that systematically assessed the thyroid hormone degree in patients afflicted by proteinuria. In our study, the thyroid function in a group of patients suffering from proteinuria was analyzed.

Materials and Methods

We investigated 74 patients with qualitatively established proteinuria without previously diagnosed thyroid disease, of whom 34 men and 40 women. Their average age is 60.9 years. A group of 20 controls were tested for free thyroxine (FT4), thyroid stimulating hormone (TSH), creatinine and albumin in serum, and quantity of urine protein.

TSH and FT4 were determined by a Roche immunological assay (sandwich principle) for in vitro quantitation of free thyrotropin and free thyroxin in human serum. Creatinine, albumin and total protein in serum, and urinary protein count, were measured by standard Hitachi 501 biochemical analyzer techniques.

The degree of glomerular filtration (GFR) was calculated using the Modification of Diet in Renal Disease (MDRD) formula. The statistical

analysis was done by using a Mann-Whitney U comparison test of the patients' results and those of the controls. We used Pearson's correlation coefficient to compare values for TSH and FT4 with those of other laboratory parameters we tested. The Pearson correlation coefficient was applied as a correlation parameter between TSH and FT4 and the concentration of the serum of other laboratory parameters. P values <0.05 were evaluated as statistically significant.

Results

We examined 74 patients with proteinuria and controls matched by age and gender. In the studied patients, the mean serum concentration of creatinine was 255 µmol/l (range 51-827), serum albumin was 31g/l (range 23-37), total protein was 65g/l (range 52-82), and proteinuria was 1.07g/l (range 0.2-11.96). In the patients with proteinuria, the mean TSH value was 2.719 mU/l (range 0.53-7.79), and FT4 was 17.04 pmol/l (range 11.39-24.95). The mean TSH value was higher in proteinuria patients than in the healthy controls (2.719 mU/l vs 1.78 mU/l). For FT4, the difference between patients with proteinuria and healthy controls was 17.04 pmol/l vs 16.39 pmol/l. By comparing the mean values of the laboratory parameters we tested in proteinuria patients and controls, we found a statistically significant difference for TSH, FT4, Crea and Alb (Table 1).

In patients with proteinuria, we found that TSH correlated negatively with serum albumin (r=0.2, p<0.003). Figure 1 shown correlation between TSH and serum albumin. We also found that TSH and FT4 did not correlate with eGFR.

Parameter	Proteinuria	Controls	p<0.05	
TSH	2.719 mU/l	1.78 mU/l	0.003	
FT4	17.04 pmol/l	16.39 pmol/l	0.005	
Crea	255 μmol/l	78 μmol/l	0.001	
Alb	31 g/l	46 g/l	0.001	

Table 1. Statistically significant differences in patients with proteinuria and controls

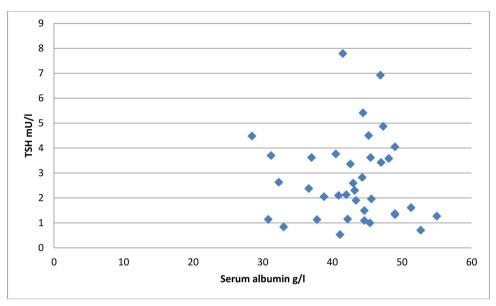


Figure 1. Correlation between serum albumin and TSH in patients with proteinuria

Discussion

In our study focused on the thyroid function of patients with proteinuria without a diagnosed thyroid disease. We showed that TSH levels in patients with proteinuria were significantly higher than those in healthy subjects without kidney disease and proteinuria (although the variations are in the reference range). This data is consistent with urinary thyroid hormone losses in patients with proteinuria, which stimulates the production of TSH. The role of proteinuria was also confirmed by the negative significant correlation between TSH and serum albumin.

Despite the fact that some studies have reported the development of growth of apparent hypothyroidism in patients afflicted by nephrotic syndrome, the prevalence of this complication remains largely ambiguous [11-13]. Subclinical hypothyroidism occurs more often in such patients [14]. Figure 1 shows that even in the patients with the nephrotic syndrome, TSH levels more often did not exceed 4 mU/l.

Lo et al. (2005) assessed thyroid function in patients suffering from renal insufficiency. The authors reported an increased incidence of subclinical hypothyroidism with elevated TSH levels in patients who had reduced GFR [14]. The loss of thyroid hormones is most likely due to the decreased level of thyroxine-binding globulin, thereby increasing the production of TSH, which is thought to originate from proteinuria [9, 15].

Conclusions

In our study, we found that patients with proteinuria had higher levels of TSH, probably due to thyroid hormone loss with the urine. These losses, however, cannot lead to a clinically proven hypothyroidism.

Acknowledgements

This study has no financial support.

References

- Branten AJW, Bufvereijken PW, KlasenIS, Bosch FH, Feith GW, HollanderDA, et al. Urinary excretion of β2-microglobulin and IgG predict prognosis in idiopathic membranous nephropathy: a validation study. J Am Soc Nephrol. 2005;16:169-74.
- Gilles R, den Heijer M, Ross AH, Sweep FC, Hermus AR, Wetzels JF. Thyroid function in patients with proteinuria. Netherlands J Med. 2008;66(11):483-5.
- Mariani LH,Berns JS.The Renal Manifestations of Thyroid Disease. J Am Soc Nephrol. 2012;23(1):22-26.
- 4. Saini V,Yadav A,Kataria M,AroraAS,Singh R. Correlation of creatinine with TSH levels in overt hypothyroidism a requirement for monitoring of renal function in hypothyroid patients?Clin Biochem.2012;45(3):212-4.
- 5. Mansournia N, Riyahi S, Tofangchiha S,

Mansournia MA, Riahi M, Heidari Z, et al.Subclinical hypothyroidism and diabetic nephropathy in Iranian patients with type 2 diabetes.J Endocrinol Invest.2017;40 (3):289-295.

- Xin Du, Binbin Pan, Wenwen Li, Yonghua Zou,Xi Hua, Wenjuan Huang, et al. Albuminuria is an independent risk factor of T4 elevation in chronic kidney disease.Sci Rep. 2017;7:41302. doi: 10.1038/srep41302.
- 7. Schussler GC.The thyroxine-binding proteins. Thyroid. 2000;10:141-9.
- Iglesias P, Diez JJ. Thyroid dysfunction and kidney disease. Eur J Endocrinol. 2009;160:503-15.
- 9. Afroz S, KhanAH, Roy DK. Thyroid function in children with nephrotic syndrome. Mymensingh Med J. 2011;20(3):407-11.
- Kapoor K, Saha A, Dubey NK. Subclinical no autoimmune hypothyroidism in children with steroid resistant nephritic syndrome. Clin Exp Nephrol. 2014;18(1):113-7.

- 11. Hoogendoorn EH, Hermus AR, de Vegt F, Ross HA, Verbeek AL, Kiemency LA, et al. Thyroid function and prevalence of anti-thyroperoxidase antibodies in a population with borderline sufficient iodine intake: Influences of age and sex. Clin Chem. 2006;52:104-11.
- 12. Lim VS. Thyroid function in patients with chronic renal failure. Am J Kidney Dis. 2001;38(Suppl 1):S80-4.
- Niloofar H, Sayed M, Behnam N.Examine of thyroid function in pediatric nrphrotic syndrome. Intern J Pediatr. 2015;3(2):59-65.
- 14. Lo JC, Chertow GM, Go AS, Hsu CY. Increased prevalence of subclinical and clinical hypothyroidism in persons with chronic kidney disease. Kidney Int. 2005;67:1047-52.
- 15. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A More Accurate Method To Estimate Glomerular Filtration Rate from Serum Creatinine: A New Prediction Equation. Ann InternMed. 1999;130(6):461-70.