

Review Article

Subclinical hypothyroidism in Chronic Kidney Disease

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ABSTRACT:

Thyroid hormones play a vital role in renal physiology and functions. Subclinical hypothyroidism has higher prevalence in chronic kidney disease (CKD) patients not requiring dialysis. It has been associated with cardiovascular risk and mortality whereas its role in CKD patients has not been well defined. Moreover, the role of thyroxin supplementation in SCH patients with CKD is controversial. The present article aims to throw light upon the interactions between SCH and CKD.

Key words: Thyroid hormones, hypothyroidism, renal disease.

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INTRODUCTION

The thyroid produces 2 major hormones- triiodothyronine (T3) and thyroxine (T4) that significantly affect the functions of all major organs of our body. Subclinical hypothyroidism which is defined biochemically as elevated TSH levels (4.5- 10 mIU/l) with normal FT4 levels¹ is found to have an estimated prevalence of 4-10% in the general population.²⁻⁴ However the prevalence of subclinical hypothyroidism in CKD patients not on dialysis is much higher and estimated at around 18%.⁵ CKD affects the pituitary-thyroid axis as well as the peripheral metabolism of thyroid hormones.⁶ Though numerous factors are found to contribute to thyroid disorders in CKD like autoimmune thyroiditis, altered iodine metabolism, resistance to thyroid hormones etc but exact mechanisms are unclear.⁵ Therefore in this article we plan to throw light on the interactions between thyroid dysfunction and CKD.

PREVALENCE

CKD is a major disease globally that affects around 5-10% of the population globally.⁷ As previously stated the prevalence of subclinical hypothyroidism is much higher in CKD patients not requiring dialysis compared to general population. The most common thyroid abnormalities in CKD patients are low T3

levels and subclinical hypothyroidism.⁶ Prevalence of subclinical hypothyroidism is found to increase with age and is more in elderly females(7-18%) compared to elderly males(2-15%).^{8,2} The progression rate from subclinical to overt hypothyroidism is 3-18% of affected patients per year.⁹ Autoimmune thyroiditis is one of the major causes of thyroid dysfunction in CKD and the prevalence of anti-TPO antibodies in SCH is around 12-70.2% as per various studies.¹⁰

PHYSIOLOGY OF THYROID DYSFUNCTION IN CKD

A number of structural and functional abnormalities are seen in the thyroid gland as the GFR declines. Normal kidney functions by means of glomerular filtration leads to iodide clearance. However impaired iodine clearance in CKD results in increased total body inorganic iodide that leads to Wolff-Chaikoff effect that blocks production of thyroid hormones.¹¹ Patients with ESRD have decreased free T3 due to decreased peripheral conversion of T4 to T3.^{12,13} However plasma rT3 levels are typically normal in these patients because the conversion of T4 to the metabolically inactive rT3 is not increased.^{12,13} Metabolic acidosis along with reduced protein binding in CKD also contributes to low T3.¹⁴ Chronic

inflammatory and malnourishment in CKD further leads to low T3.¹⁵

TSH levels in CKD also rise due to effect of thyrotropin from pituitary which is caused by uremia.¹⁶ Moreover the circadian rhythm of TSH is lost along with its compromised bioactivity due to poor glycosylation.¹⁵ Use of heparin in dialysis results in transient rise in serum T4 levels that occurs during hemodialysis.¹⁷

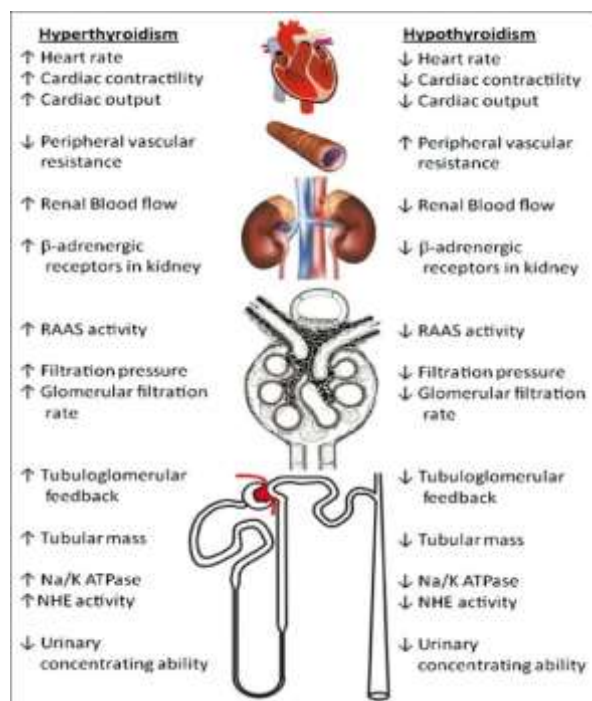


Figure 1: Effects of hypothyroidism and hyperthyroidism on renal physiology¹⁸

CLINICAL SIGNIFICANCE

Thyroid abnormalities are associated with a spectrum of health hazards. Dyslipidemia is seen in thyroid dysfunction and is milder at TSH values between 5-10 mIU/L as compared to TSH values >10 mIU/L.^{19,20} While overt and subclinical hypothyroidism is known to increase the risk for cardiovascular disease (especially in elderly females), the cardiovascular risk among patients with coexistent CKD and subclinical hypothyroidism is yet to be determined.⁶ Various studies have found that TSH levels are higher in patients with proteinuria (probably due to loss of thyroid hormones in urine).²¹ However, no evidence supporting association of hypoalbuminemia and endocrinal abnormalities in CKD has been found yet.²²

Role of thyroxine supplementation in subclinical hypothyroidism in CKD remains controversial. Decreased thyroid dysfunction in CKD is considered as an adaptation to minimise protein catabolism in CKD.⁶ Multiple attempts done to correct thyroid dysfunction CKD via thyroxine replacement resulted in negative nitrogen balance and increased protein catabolism.²³

CONCLUSION

Subclinical hypothyroidism is more prevalent in patients of CKD not on dialysis. SCH is associated with increased cardiovascular mortality especially in elderly but its cardiovascular risk in CKD is yet to be determined. Role of thyroxin supplementation in SCH patients with CKD is unclear and further studies are needed in this direction.

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