Kidney Res Clin Pract 35 (2016) 165–168

Kidney Research and Clinical Practice

journal homepage: http://www.krcp-ksn.com
Contents lists available at ScienceDirect

Original Article

Prevalence of hypothyroidism in patients with chronic kidney disease: a cross-sectional study from North India

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Article history:
Received 15 March 2016
Received in revised form
17 May 2016
Accepted 20 June 2016
Available online 26 July 2016

Keywords:
Chronic kidney disease
Hypothyroidism
Prevalence

A B S T R A C T

Background: There is an increased prevalence of hypothyroidism in chronic kidney disease (CKD) patients as the glomerular filtration rate falls. However, there is a paucity of Indian data in this respect.

Methods: A cross-sectional analysis was performed based on the database of the information system of a tertiary care hospital in northern India to retrieve results of nephrology CKD outpatients (> 18 years of age) from September 2013 to October 2015 to determine the prevalence of hypothyroidism in the non–dialysis-dependent CKD population. Overt hypothyroidism was defined by a thyroid-stimulating hormone (TSH) level > 5.5 mIU/L and free T4 level < 0.89 ng/dL with clinical symptoms. Subclinical hypothyroidism was defined by a TSH level > 5.5 mIU/L and a free T4 level ≥ 0.89 ng/dL.

Results: Among 1,863 CKD patients, 358 patients underwent biochemical analysis for hypothyroidism. Among these, 143 had biochemical subclinical hypothyroidism and 59 had overt hypothyroidism. Patients in the overt hypothyroid group had significantly higher TSH levels and a lower free T4 level than those in the non-hypothyroid group. Patients with hypothyroidism (both clinical and subclinical) had significantly lower serum albumin and serum calcium levels than those in the non-hypothyroid group. Intact parathyroid hormone was also significantly higher in the hypothyroid groups. An increased prevalence of hypothyroidism was observed in patients with a reduction in the glomerular filtration rate.

Conclusion: There is growing evidence of increased prevalence of hypothyroidism in dialysis-independent CKD patients. A number of findings such as lower serum albumin, serum calcium, and hemoglobin levels and higher intact parathyroid hormone levels are seen in this group. Specific treatment can help improve these. Hence, there is a need to formulate guidelines to screen this population for hypothyroidism.

Introduction

It has been shown that in chronic kidney disease (CKD), as the glomerular filtration rate (GFR) falls, there is a higher possibility of developing clinical and subclinical hypothyroidism (SCH) [1]. With falling GFR, there are a number of abnormalities developing in the thyroid gland at both structural and functional level. There is an increase in thyroid volume as the

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http://dx.doi.org/10.1016/j.krcp.2016.06.003

GFR falls [2]. Low T3 syndrome is also commonly seen in CKD population, which is possibly an adaptation of the chronic inflammatory and malnourished state prevalent in these patients. The overlapping features of CKD and hypothyroidism make it all the more challenging for the clinician to timely diagnose and treat it. In spite of the growing volume of information, there is a dearth of Indian data with respect to SCH and overt hypothyroid prevalence in patients with CKD who are not dialysis dependent. To gain further insight into this, we conducted a survey of the CKD population visiting this tertiary care center to determine the prevalence of hypothyroidism in the non–dialysis-dependent CKD population.

Methods

A cross-sectional analysis based on the database of the information system of a tertiary care hospital in northern India to retrieve results of nephrology CKD outpatients (> 18 years of age) referred to this tertiary care center from September 2013 to October 2015 was conducted.

Serum thyroid-stimulating hormone (TSH) and free T4 (FT4) concentrations were quantified by direct chemiluminescence using acridinium ester technology on the ADVIA Centaur XP analyzer (Siemens Healthcare, Tarrytown, New York, USA). Functional sensitivity for TSH and FT4 was quoted by the manufacturer as 0.004–150 mIU/L and 0.1–12.0 ng/dL, respectively. Reference values in our laboratory were 0.35–5.5 mIU/L for TSH and 0.89–1.78 ng/dL for FT4, respectively. The estimated GFR (eGFR) was calculated using the 2009 chronic kidney disease Epidemiology Collaboration creatinine equation, and the stages of CKD were defined according to the kidney disease improving global outcome guidelines for evaluation of CKD.

Overt hypothyroidism would be defined by a TSH level > 5.5 mIU/L and a FT4 level < 0.89 ng/dL with clinical symptoms. SCH would be defined by a TSH level > 5.5 mIU/L and a FT4 level ≥ 0.89 ng/dL (the lower limit of the normal range).

Inclusion criterion was all CKD patients (> 18 years of age) not requiring long-term dialysis with TSH levels > 5.5 mIU/L.

Exclusion criteria were as follows: subjects younger than 18 years, pregnant women, subjects receiving concurrent treatment with drugs that could contribute to hypothyroidism, and subjects receiving antithyroid drugs presumably for hyperthyroidism.

All secondary cases of hypothyroidism and subjects in whom kidney functions could not be estimated because of missing serum creatinine values or those in whom TSH or FT4 levels were not available were also excluded.

Statistical analysis

Data were analyzed using SPSS 16 (IBM Corporation, New York, USA). The Student *t* test, analysis of variance (one way), Mann–Whitney test for scattered data were performed, and odds ratio with 95% confidence interval is reported. A *P* value < 0.05 was considered significant.

Results

Study population

A total of 1,863 adult participants had valid serum creatinine measurements and eGFR. Among 1,863 CKD patients seen in the nephrology out patient department, 358 patients underwent biochemical analysis for hypothyroidism. Among these, 156 had normal TSH values (between 0.35 and 5.5 mIU/L), whereas 143 had biochemical SCH (i.e., TSH > 5.5 mIU/L with normal FT4 levels), and 59 had overt hypothyroidism (i.e., TSH > 5.5 mIU/L with FT4 levels < 0.89 ng/dL). The prevalence of subclinical and overt primary hypothyroidism together in the total CKD population was 10.84%, whereas it was 56.42% in the subjects tested for hypothyroidism (Fig. 1 and Table 1).

The mean age was 55.89 ± 12.85 and 55.16 ± 14.28 years in the subclinical and overt hypothyroidism groups, respectively.

Characteristics of persons with and without prevalent hypothyroidism

Overall, individuals with clinical hypothyroidism and SCH were roughly of the same age (Table 2). In gender distribution between the groups, the number of men was higher in the overt hypothyroid group although nonsignificant. In the subclinical hypothyroid group, both the sexes were almost equally distributed. Systolic blood pressure was significantly higher in overt and subclinical hypothyroid groups compared to the nonhypothyroid group ($P < 0.001$).

FT4 concentrations differed significantly among the overt, subclinical hypothyroid, and nonhypothyroid groups (0.7 ± 0.1, 1.2 ± 0.2, and 1.3 ± 0.2 mIU/L, respectively, $P = 0.001$). Mean spot urine protein of 134.8 ± 129.8 mg/dL (median 100 mg/dL) was significantly higher in the overt hypothyroid group ($P < 0.02$). Patients with hypothyroidism (both clinical and subclinical) had significantly lower serum albumin ($P = 0.00$) and serum calcium levels ($P = 0.002$) than those in the nonhypothyroid group. Intact parathyroid hormone (PTH) was also significantly higher in the hypothyroid groups than in the nonhypothyroid group ($P = 0.001$). Hemoglobin levels were lower in the hypothyroid groups than in the nonhypothyroid group although it was not significant ($P = 0.068$). The patients in the hypothyroid groups (both clinical and subclinical) also had higher BMI compared with patients in the nonhypothyroid group (24.7 ± 6.5 vs. 23.0 ± 5.8). No significant difference was seen in the lipid profile among all the groups.

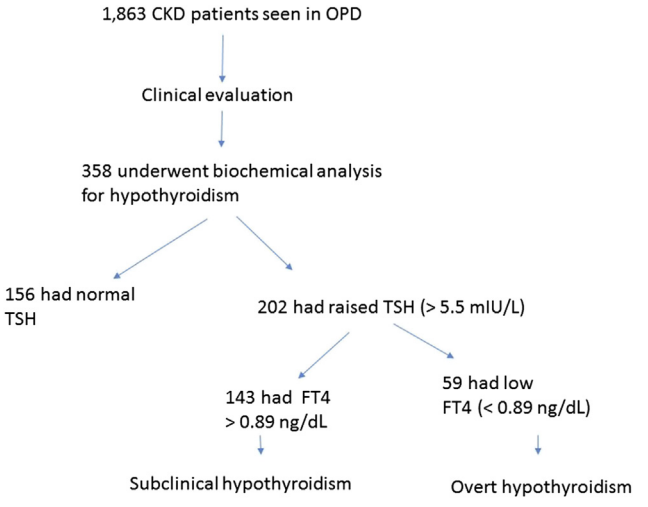

Figure 1. Flow chart of study design.
CKD, chronic kidney disease; FT4, free T4; OPD, out patient department; TSH, thyroid-stimulating hormone.