

## Original Article

# Assessment of Thyroid Dysfunction as a Predisposing Factor for Asymptomatic Bacteriuria in Women of Reproductive and Postmenopausal age

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## Abstract

**Background:** Infectious diseases are associated with thyroid autoimmune disorders, mainly. Meanwhile, thyroid gland function as a risk factor for infectious diseases is a challenging debate topic that needs more evaluation. Considering the high burden of hypo and hyperthyroidism in many regions of the world and the consequences of these disorders on different aspects of human health, evaluating and screening high-risk populations and treating patients is of great importance. In the present research, we investigated any association between thyroid dysfunction and asymptomatic bacteriuria in women of reproductive and postmenopausal age.

**Materials and Methods:** The study was performed for six years (between 2015-2021) in Tehran, Iran. Our study enrolled 188 women of reproductive and postmenopausal age with and without asymptomatic bacteriuria. All participants' thyroid stimulating hormone (TSH) and free T4 levels were evaluated. The association between thyroid dysfunction and asymptomatic bacteriuria was assessed.

**Results:** The mean level of TSH in all culture-positive samples was 2.39, while it was 3.11 in culture-negative samples (P value < 0.05). The mean TSH level was 2.4 and 2.3 in *Escherichia coli* and Non-*E. coli* positive urine cultures, respectively (P value= 0.67). Asymptomatic bacteriuria was significantly more common in patients with lower TSH levels. The mean level of free T4 in all participants was 8.21, with maximum and minimum levels of 12.3 and 4, respectively. Also, the mean level of free T4 in all culture-positive samples was 9.53, while 7.13 in culture-negative samples (P value=0.09). The mean free T4 level was 9.36 and 10.03 in *E. coli* and Non-*E. coli* positive urine culture respectively (P value= 0.35).

**Conclusion:** Our study revealed a significant correlation between the population's TSH level and asymptomatic bacteriuria. Also, it showed no significant association between TSH level and any specific uropathogenic.

**Keywords:** Thyroid dysfunction, Bacteriuria, Women

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## Introduction

The association of thyroid hormones and the function of the immune system is an exciting issue debated for many years. The thyroid hormones have a wide range of effects on the human body. Some of these functions influence metabolic, cardiovascular, and developmental status. The thyroid hormones may also play a role in maintaining normal immune function and preventing infectious diseases. The association between thyroid function and infectious diseases has been addressed in many researches. In a recent analysis in 2020, the authors concluded that the presence of thyroid disease should be regarded as an essential factor in future risk stratification models for coronavirus disease 2019 (COVID-19)<sup>1</sup>. In another study in 2016, the authors addressed the role of thyroid disease in susceptibility to infectious diseases. They mentioned that patients experiencing a thyroid storm are at a higher infection risk because an overactive metabolic state acts as a catalyst to delay the neutrophil response toward sites of infection<sup>2</sup>.

Considering the fundamental role of the immune system in preventing infectious diseases and the impact of thyroid activity and thyroid hormones on the immune system, hypo or hyperthyroid patients may be more prone to acute bacterial and viral infection. A systematic review and meta-analysis in 2018 evaluated the possibility of decreased thyroid hormones as a prognostic factor of mortality in sepsis<sup>3</sup>. This meta-analysis suggested that the decreased thyroid hormone during intensive care unit (ICU) admission might be associated with increased mortality in adult septic patients. The impact of thyroid dysfunction, specifically on the urinary tract, was addressed in a case report that evaluated the association of subclinical hypothyroidism and recurrent urinary tract infection. Based on this research, hypothyroidism and hyperthyroidism affect renal function through direct renal and systemic hemodynamic, metabolic, and cardiovascular effects. The relationship between subclinical hypothyroidism and recurrent urinary infections is controversial, but according to this study, there are benefits in controlling thyroid hormones<sup>4</sup>. This study addressed any association between thyroid dysfunction and asymptomatic bacteriuria in women of reproductive and postmenopausal age.

## Methods

**Study Design and Setting:** The present research was a cross-sectional study on 188 patients with and without asymptomatic bacteriuria referred to Negaresh pathobiology laboratory for a routine screening evaluation. Bacteriuria was diagnosed when a significant colony-forming unit (CFU) of a bacteria was cultured from appropriately collected urine samples. Samples that contained  $\geq 10^5$  CFU of the urinary pathogen/ml of pure culture were considered positive. Blood agar, MacConkey agar, and Eosin methylene blue plates were used for pathogen identification and differentiation. Thyroid-stimulating hormone (TSH) and free T4 levels of all patients were analyzed accordingly. This study was approved by the Ethics Committee of the Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC1399.636) in Tehran, Iran.

**Definition:** The term asymptomatic bacteriuria refers to the isolation of bacteria at specified quantitative counts ( $\geq 10^5$  colony-forming units) in an appropriately collected urine specimen from an individual without symptoms of urinary tract infection. The normal range of TSH is 0.39-6.16  $\mu$ IU/ml, and the normal range of T4 is 4.4-10.8  $\mu$ g/dl and 4.8-11.6  $\mu$ g/dl in males and females, respectively.

**Participants:** In 6 years (between 2015-2021), 188 women of reproductive and postmenopausal age (age above 15) with and without asymptomatic bacteriuria were enrolled in our study. All participants had no signs or symptoms of urinary tract infection. The exclusion criteria were as follows: 1) use of any antibacterial agent within the last three months, 2) chronic renal failure, 3) nephrolithiasis, 4) spinal cord injuries, 5) history of surgical procedure in urinary tract within the last three months, 6) presence of indwelling urinary catheters, 7) pregnancy, 8) use of immunosuppressive agents, 9) gynecological disorders, 10) urinary tract stent or nephrostomy tube, and 11) symptomatic patients.

**Statistical analysis:** The association between TSH and Free T4 level and asymptomatic bacteriuria was evaluated using SPSS version 23 (IBM, New York, USA). Kolmogorov-Smirnov test was performed to evaluate the normal distribution of data.

## Results

A total of 700 medical records were evaluated in our assay. After excluding documents with missing data and other exclusion criteria, 188 women with and without asymptomatic bacteriuria were enrolled in the study. We evaluated TSH and free T4 levels in positive and negative urine samples and analyzed the association of specific uropathogen with TSH and free T4 in patients with asymptomatic bacteriuria. All study participants were female. The mean age of women participating in our study was 49, with maximum and minimum ages of 91 and 16, respectively. The mean age of women with positive urine culture was 59 and 40 for negative urine samples. 44.7 percent of participants had positive urine cultures. *Escherichia coli* (*E. coli*) was the major pathogen in the positive urine culture, accounting for 75 percent of infections. *Klebsiella pneumoniae* was the second pathogen isolated from urine samples, accounting for 17 percent of infections. The remaining uropathogens included *Staphylococcus saprophyticus*, *Enterococcus*, and *Enterobacter*, accounting for 8 percent of infections. The mean TSH level of all participants was 2.79, with maximum and minimum levels of 27.1 and 0.1, respectively. The mean level of TSH in all culture-positive samples (including *E. coli* and non-*E. coli*-positive samples) was 2.39, while it was 3.11 in culture-negative samples (P value < 0.05). The mean TSH levels were 2.4 and 2.3 in *E. coli* and Non-*E. coli* positive urine cultures, respectively (P value= 0.67) (Figure 1). Asymptomatic bacteriuria was significantly more common in patients with lower TSH levels. However, the mean TSH level in *E. coli*

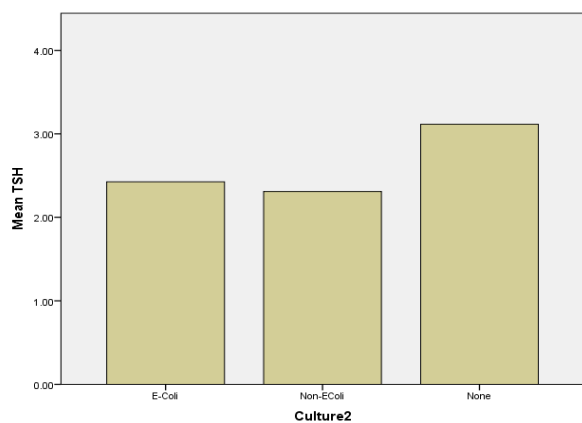


Figure 1. Correlation of culture with TSH level.

and Non- *E. coli*-positive urine cultures had no significant difference. The mean level of free T4 in all participants was 8.21, with maximum and minimum levels of 12.3 and 4, respectively. Also, the mean level of Free T4 in all culture-positive samples was 9.53, while it was 7.13 in culture-negative samples. (P value =0.09). The mean free T4 level was 9.36 and 10.03 in *E. coli* and Non- *E. coli* positive urine cultures, respectively (P value=0.35) (Figure 2). These data revealed a significant correlation between TSH level (but not T4 level) and asymptomatic bacteriuria in the studied population. Also, they showed no significant association between TSH level and any specific uropathogen.

## Discussion

We evaluated any association between thyroid dysfunction, TSH, Free T4, and asymptomatic bacteriuria in women of reproductive and postmenopausal age. We also evaluated the association of any specific uropathogen with TSH and Free T4 in the study population with a positive culture. Considering the potential progression of asymptomatic bacteriuria to frank urinary tract infection (UTI), eliminating any risk factor for asymptomatic bacteriuria may lower the chance of developing UTI.

The innate immune system in the urinary tract leads to the expression of a different range of pattern recognition receptors which enable early recognition of the pathogen and have an essential role in preventing infection. When uropathogens invade the urinary tract, innate immune cells start signaling cascades that lead to local immune responses, eventually preventing

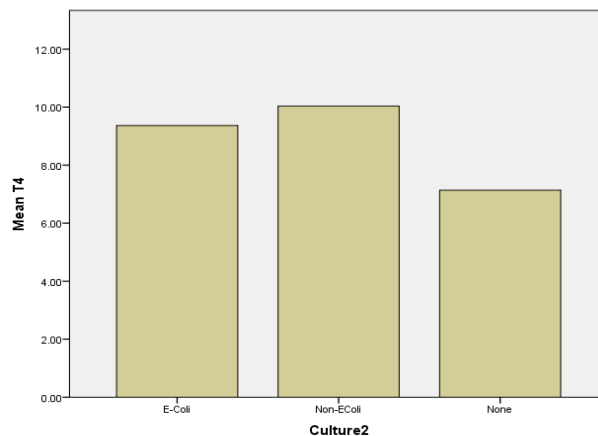


Figure 2. Correlation of culture with T4 level.

infection. Thyroid hormones can probably influence the functioning of the innate and adaptive arms of the immune system in the urinary tract, leading to more vulnerability to asymptomatic bacteriuria and, perhaps, frank urinary tract infection (UTI).

The impact of thyroid dysfunction on vulnerability to infection, specifically urinary tract infection, is a controversial topic that needs more investigation. In an animal and prospective cohort study in 2020, the authors evaluated the association of hyperthyroidism and subclinical bacteriuria in cats. In conclusion, the article revealed that hyperthyroid cats were not at risk for subclinical bacteriuria<sup>5</sup>.

In contrast to the study mentioned above, in another survey in 2013, the authors indicated an association between hyperthyroidism and bladder pain syndrome/interstitial cystitis. They suggested clinicians treating female subjects with hyperthyroidism be alert to urinary complaints in this population<sup>6</sup>. The association of thyroid dysfunction and chronic inflammatory diseases such as hidradenitis suppurativa was addressed in another cross-sectional research in 2021. This large-scale population-based study revealed that hidradenitis suppurativa was independently associated with hypothyroidism<sup>7</sup>.

The term asymptomatic bacteriuria refers to the isolation of bacteria at specified quantitative counts ( $\geq 10^5$  colony-forming units) in an appropriately collected urine specimen from an individual without symptoms of urinary tract infection. Asymptomatic bacteriuria does not lead to hypertension, chronic renal failure, or decreased survival, but it is uncommonly followed by symptomatic infection and frank UTI. Asymptomatic bacteriuria is a marker for poor overall health status in people with diabetes and elderly inpatients. In contrast, asymptomatic bacteriuria in pregnancy (4%–7% incidence) is associated with progression to symptomatic pyelonephritis (Wing et al., 2014). In an investigation that was conducted to determine risk factors for infectious complications after a urodynamic study in women, Mônica Martins Nóbrega et al. concluded that The rate of infectious complications after the urodynamic study was low, and advanced pelvic organ prolapse and hypothyroidism increased the risk for bacteriuria.

However, only BMI >30 was associated with bacteriuria and UTI after a urodynamic study<sup>8</sup>.

## Conclusion

Our study revealed a significant correlation between TSH level (but not T4 level) and asymptomatic bacteriuria in the studied population. Also, it showed no significant association between TSH level and any specific uropathogen.

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## Conflict of interest

The authors further declare that they have no conflict of interest.

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