



# **The Prevalence Subclinical Hypothyroidism Among Iranian Pregnant Women: A Systematic Review and Meta-analysis**

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## **Abstract**

### **Objective**

The present meta-analysis was conducted to evaluate the prevalence of thyroid dysfunctions among Iranian pregnant women.

### **Methods**

Two reviewers independently reviewed the titles and abstracts of all identified records. At this stage, duplicate and unrelated studies were excluded.

### **Results**

Four eligible studies evaluating evaluate the prevalence of thyroid dysfunctions among Iranian pregnant women were used for meta-analysis. According to the results of the present study, the most prevalent thyroid disorder among Iranian pregnant women was subclinical hypothyroidism with a prevalence of 25%(95%CI:24% -27%), while the prevalence of overt hypothyroidism was 2%(95%CI:1%-2%)

### **Conclusion**

The present study provides comprehensive information on thyroid disease status to policymakers and clinicians. The results of this meta-analysis revealed a high prevalence of thyroid disorders, especially hypothyroidism. The decision to recommend thyroid screening during pregnancy for all women is still debated since the positive effects of treatment on pregnancy outcomes need to be assured. Also, the evidence on the effect of thyroid screening and treatment of thyroid disorders on pregnancy outcomes is still insufficient. However, a large percentage of general practitioners, obstetricians, and gynecologists in Iran perform the screening procedures.

**Keywords:** Hypothyroidism, Pregnancy, Thyroid dysfunction

## Introduction

Thyroid disorders are considered the second most common endocrine disorder in women at reproductive age (1). Hypothyroidism is the most common thyroid dysfunction in pregnancy with a prevalence of 2 to 5% (2, 3). According to the previous reports, the prevalence of hypothyroidism (both overt and subclinical) in Iranian pregnant women is estimated at 4.7% (4). Several studies have evaluated the adverse effects of overt hypothyroidism (OH) on pregnancy outcomes (5-7), although there is conflicting opinions regarding the adverse fetal-maternal effects of subclinical hypothyroidism (8). Proper screening can lead to early diagnosis of these disorders in pregnancy. However, universal screening for thyroid dysfunction in pregnancy is a controversial issue (9, 10).

Although the complications of hypothyroidism or overt hyperthyroidism in pregnancy outcomes and neonatal and childhood development have been well documented (11-16), there is still no consensus on the association between subclinical thyroid disorders or increased thyroid antibodies and complications in pregnancy and childhood. Some studies suggest that subclinical hypothyroidism and thyroid autoimmunity are associated with adverse maternal and fetal outcomes (16-20). It has even been reported that hypothyroid women with abnormally elevated levels of serum thyroid antibodies are at risk of adverse outcomes of pregnancy such as spontaneous and premature abortion (13,15,17), while others have documented opposite results (20,21).

Several studies have been carried out regarding thyroid dysfunction in pregnant women in Iran (22-39). However, these studies have provided different results, so that the prevalence of hypothyroidism ranged from 0.4 to 34.4% and that of hyperthyroidism ranged from 0.7 to 16.7% (40-42). Since meta-analyses combine multiple studies with the same objective and can provide a more reliable estimate by increasing the sample size and decreasing the confidence interval, the

present meta-analysis was conducted to evaluate thyroid dysfunction among Iranian pregnant women.

## Methods

International online databases, including Web of Science, Ovid, Science Direct, Scopus, EMBASE, PubMed/Medline, Cochrane Database of Systematic Reviews - CDSR, EBSCO, CINAHL, as well as national databases, including Magiran (<http://www.magiran.com/>), Scientific Information Database (SID) (<http://www.sid.ir/>), Regional Information Center for Science and Technology (RICST) (<http://en.ricest.ac.ir/>), Barkat knowledge network system (<http://health.barakatks.com>), Civilica (<https://www.civilica.com/>), National Library of Iran (<http://www.nlai.ir/>) Iranians Research Institute of Science and Information Technology (IranDoc (<https://irandoc.ac.ir>) and elmnet (<https://elmnet.ir>) were examined. Google Scholar was also used to retrieve online articles in this area, which may have been removed from online databases to increase the comprehensiveness of the search.

A combined search was performed based on the keywords of "prevalence", "epidemiology", "frequency", "pregnant", "pregnancy", "pregnancy", "prenatal care", "thyroid", "hypothyroid", "hyperthyroid", "peroxidase antibody", "TPOAb" and "Iran" using Boolean operators (AND/OR). Finally, the references in the retrieved articles were also reviewed. An example of a combined search in the PubMed database is as follows: (prevalence or epidemiology or frequency or incidence) [all terms] and (pregnant or pregnancy or prenatal care) [all terms] and (thyroid or hypothyroidism or hyperthyroidism or peroxidase antibody or TPOAb) [all terms] and (Iran)

## Selection of study and data extraction

Two reviewers independently reviewed the titles and abstracts of all identified records. At this stage, duplicate and unrelated studies were

excluded. Duplicate articles were identified manually or using the EndNote X7 program. Then, both reviewers independently screened the articles to identify eligible studies based on the inclusion and exclusion criteria. Both reviewers independently extracted the data. Any disagreement between data extractors was resolved by consensus or by a third author.

### Statistical analysis

I<sup>2</sup> index and Q test were used to evaluate the difference in studies. Its value may vary from 0 to 100 percent, and the values of 75, 50, and 25 percent indicate high, moderate, and low heterogeneity, respectively, among the studies. In addition,  $P < 0.1$  was used to determine heterogeneity. Due to high heterogeneity of the studies, we performed a meta-analysis based on the random effects model and reported the results based on the pooled prevalence and 95% confidence interval (CI). Heterogeneity among the studies was detected based on meta-regression and subgroup analysis. Sensitivity analysis was performed by excluding one study at a time to assess the consistency of the results. To evaluate

the publication bias, funnel plots and Begg and Egger tests were used. All analyses were performed using version 2 of comprehensive meta-analysis software.

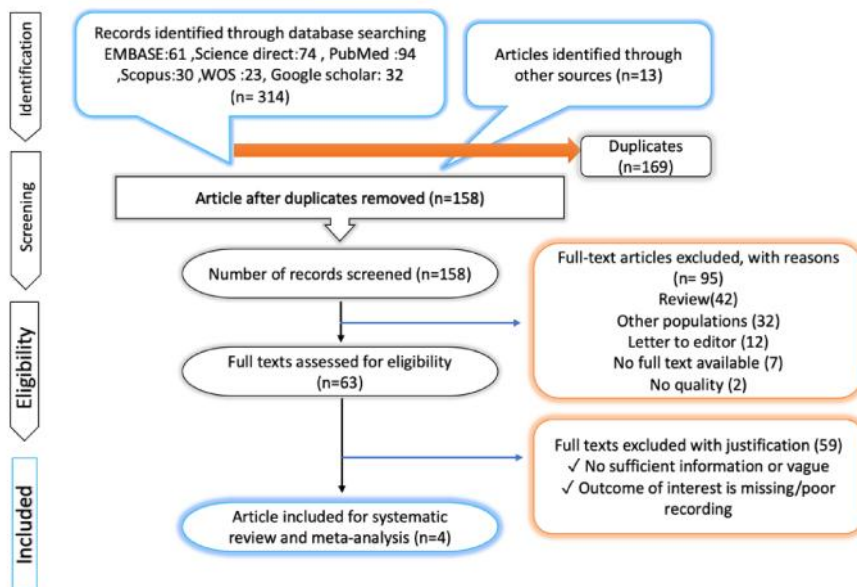
### Results

We identified 327 potential articles from the databases and 158 articles remained after excluding the duplicate and unrelated studies. After reviewing the full text, 95 articles were excluded for at least one of the following reasons: review(42), other population(32), letter to the editor(12), no full text(7), and no quality(2). This process is shown in Figure 1. Finally, 4 eligible studies were used for meta-analysis (Table 1).

### Meta-analysis

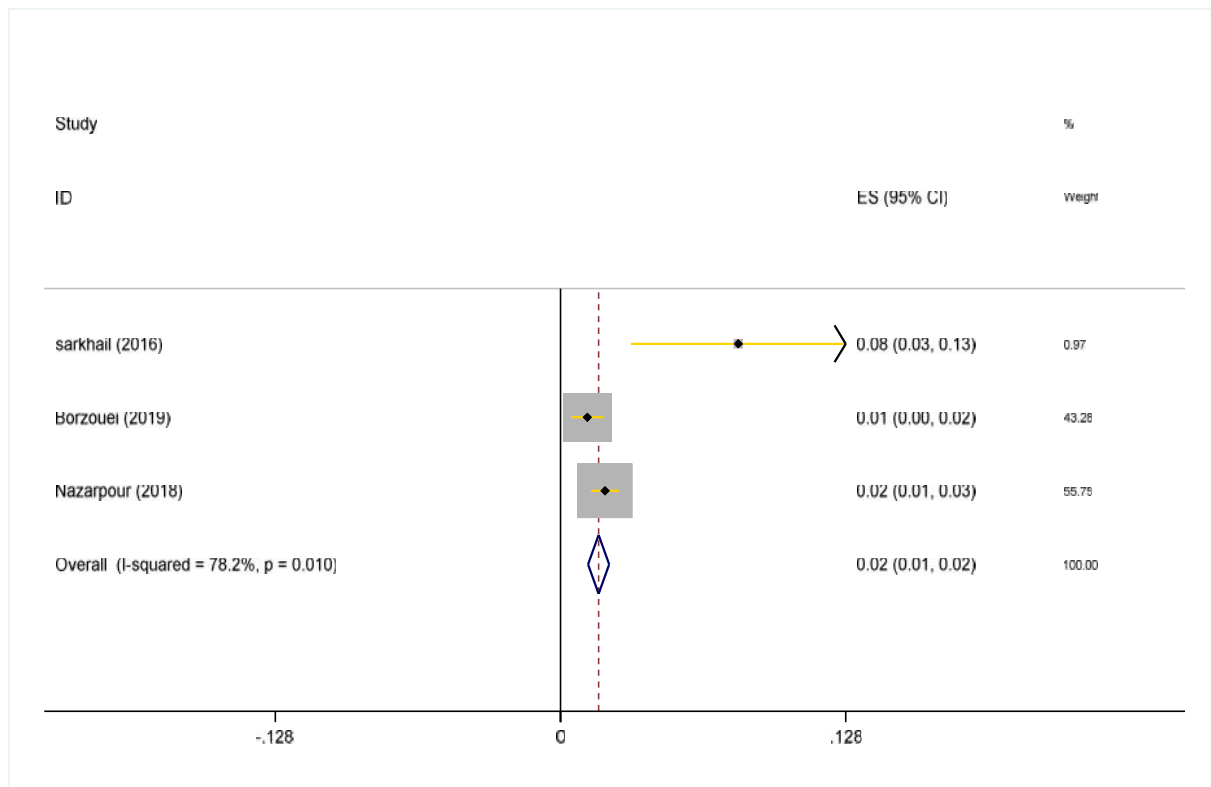
According to the results of the present study, the most prevalent thyroid disorder among Iranian pregnant women was subclinical hypothyroidism with a prevalence of 25%(95%CI:24% -27%), while the prevalence of overt hypothyroidism was 2%(95%CI:1%-2%)(Figure2,3)

Figure1. PRISMA flow diagram



**Table1. The study characteristics regarding the prevalence of different types of thyroid disorders among Iranian pregnant women**

Author	Year	Province	design	Sample size	Mean age	hypothyroidism	hyperthyroidism	Subclinical hypothyroidism	Subclinical hyperthyroidism
Sarkhail	2016	Tehran	N/A	120	22.0±4.8	0.8%	2.5%	15%	8%
<b>Borzouei</b>	2019	Hamadan	Cross-sectional	852	27.06±5.59	1.2%	0.5%	26.5%	0.2%
Nazarpour	2018	Tehran	Prospective	1843	26.68 ± 5.30	38/1843	N/A	541/1843	N/A
Lotfalizade	2017	Mashhad	Prospective	1000	N/A	N/A	N/A	21%	N/A



**Figure 2. Meta-analysis of the prevalence of hypothyroidism in Iranian pregnant women**

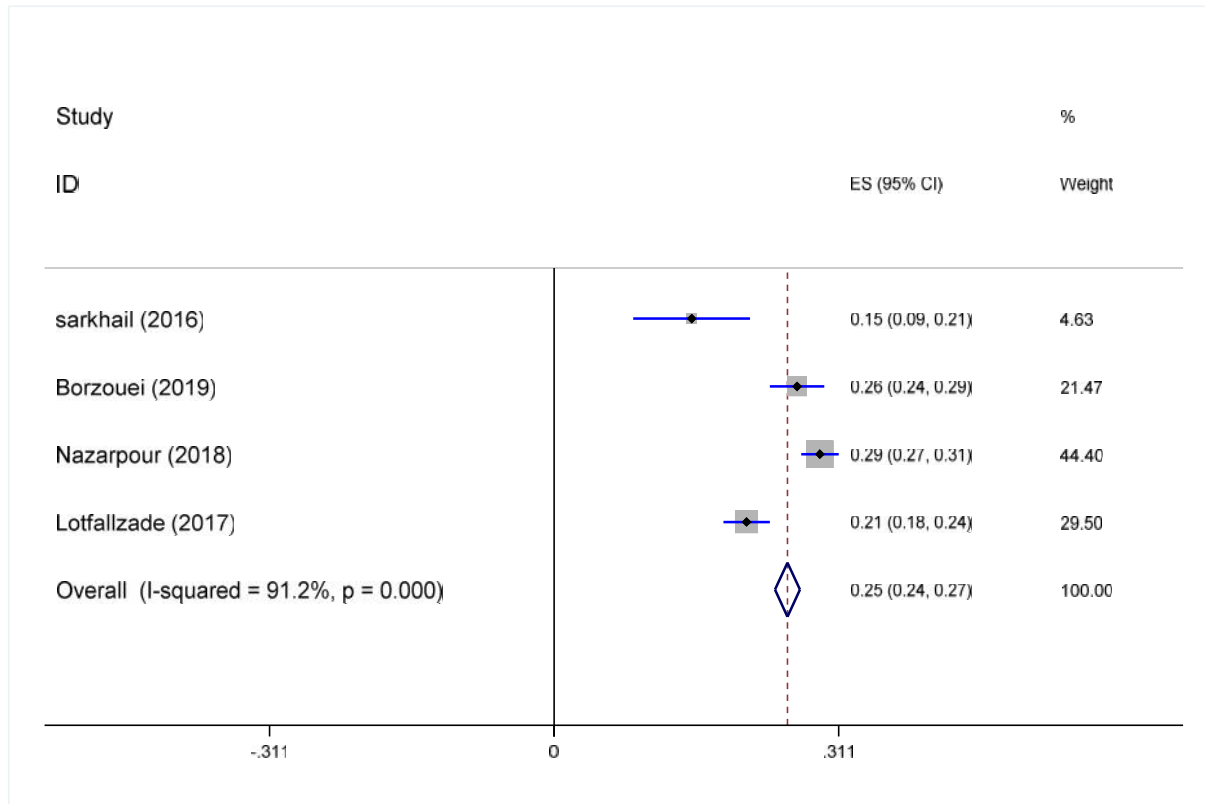


Figure 3. Meta-analysis of the prevalence of subclinical hypothyroidism in Iranian pregnant women

## Discussion

The in vitro enhanced chemiluminescence method used in this study, VitrosECi, is an ortho clinical diagnostics that is approved by FDA. The value of the first quarter is more important than the second and third quarters. Since it plays a crucial role in preventing maternal complications, if subclinical hypothyroidism is diagnosed early, treatment with low-dose levothyroxine can prevent it. The upper limit for defining the reference value of the first trimester has been discussed in the guideline (43). The special group recommends that defining the reference range should be according to the results for that particular population and the laboratory technique of that institution. If an internal or transmissible pregnancy-specific TSH reference range is not available, a higher reference limit of ~4.0 mU/L may be used. For most assays, this limit falls below the non-pregnant TSH upper reference limit of ~0.5 mU/L. In the present study, the prevalence of subclinical hypothyroidism, and overt hypothyroidism, in pregnancy were 25%, and 2%, respectively, which is comparable to

the prevalence observed in the studies by Weiwei Wang et al. (10.2%) (44) and Ajmani et al. (13.25%) (45). Variations in different areas might be due to non-uniformity in the study environment or laboratory techniques, personal human error, and differences in sample size. In India, the prevalence of hypothyroidism in pregnancy is much higher compared to western countries. Iodine deficiency may be one of the reasons. Based on the Iodine Network Global Scorecard in 2010, the percentage of households consuming iodized salt in India was 51% (46). Hashimoto's thyroiditis is the cause of hypothyroidism in iodine-sufficient regions such as North America and Western Europe. In the present study, the prevalence of subclinical hypothyroidism, and overt hypothyroidism in pregnancy was reported at 25% and 2% respectively. This result is consistent with the results of some Indian studies, in which the prevalence of subclinical hypothyroidism and overt hypothyroidism was reported at 6.1% and 0.7%, respectively (47).

Another study in India in 2016 reported a prevalence of subclinical hypothyroidism at 8% in the third trimester (48). In a recent review and meta-analysis, the prevalence of overt hypothyroidism, subclinical hypothyroidism, and isolated hypothyroxinemia was reported at 0.50%, 3.47%, and 2.05%, respectively (49).

## Conclusion

The present study provides comprehensive information on thyroid disease status to policymakers and clinicians. The results of this meta-analysis revealed a high prevalence of thyroid disorders, especially hypothyroidism. The decision to recommend thyroid screening during pregnancy for all women is still debated since the positive effects of treatment on pregnancy outcomes need to be assured. Also, the evidence on the effect of thyroid screening and treatment of thyroid disorders on pregnancy outcomes is still insufficient. However, a large percentage of general practitioners, obstetricians, and gynecologists in Iran perform the screening procedures.

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How to cite this article:

Batool Shahraki Mojahed. (2022). The Prevalence Subclinical Hypothyroidism Among Iranian Pregnant Women: A Systematic Review and Meta-analysis. Int. J. Adv. Res. Biol. Sci. 9(9): 172-180.

DOI: <http://dx.doi.org/10.22192/ijarbs.2022.09.09.016>