

Ultrasonography of Incidental Thyroid Nodules: A Systematic Review and Meta-analysis of Prevalence

CME
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Abstract

Background: An increasing number of physicians use ultrasound (US) to evaluate the thyroid. Consequently, many individuals in the general population have been diagnosed with thyroid nodules. However, there has been no systematic review examining the prevalence of incidental thyroid nodules among asymptomatic adults or elucidating the associated factors. **Methods:** We searched the MEDLINE and Embase databases to identify studies focused on thyroid incidentaloma observed through the US. **Results:** A total of 95,394 adults were enrolled, and 35,971 people were found to have thyroid incidentaloma through the US. The results revealed that the prevalence of incidentaloma was 30.6% (95% confidence interval: 26.3–36.3, $I^2 = 99\%$, $P < 0.01$). The subgroup analysis indicated that the prevalence rates of thyroid incidentaloma were 34% and 23% for females and males, respectively. The prevalence of thyroid incidentaloma was 42% and 20% for individuals aged more than 50–55 and <50–55 years, respectively. The prevalence of thyroid incidentaloma was 60% and 25% for high-frequency (>12 MHz) and low-frequency US, respectively. The majority of thyroid incidentalomas were smaller than one centimeter and had singular nodules. **Conclusion:** According to this systematic review and meta-analysis, up to 30% of asymptomatic adults will have thyroid incidentalomas detected by the US. More thyroid incidentalomas were found in women, older people, and those with a higher-frequency US.

Keywords: Incidentaloma, thyroid nodules, ultrasound

INTRODUCTION

Thyroid nodules are among the most common clinical thyroid disorders. A thyroid nodule is defined as an abnormal growth of thyroid cells and is found as a lump in the thyroid glands. The incidence of thyroid nodules is associated with sex, age, iodine deficiency, radiation exposure, and geographic area.^[1]

In addition, the prevalence of thyroid cancer is increasing worldwide. The increase in incidence might be due to age, sex, and widespread use of ultrasound (US) to examine the neck lesions including the thyroid gland. The overdiagnosis of thyroid cancer in South Korea is due to opportunistic thyroid US examinations, which are provided as an additional service in the national screening program.^[2] Overdiagnosis and

treatment can make these patients become injured and subject them to unnecessary harm and lifelong treatment. There has also been an increase in the incidence of thyroid cancer in Taiwan, thus suggesting that Taiwan is no exception to the worldwide trend of overdiagnosis of thyroid cancer.^[3]

The US is a useful tool for examining the thyroid glands. An increasing number of physicians use the US to assess the thyroid. Subsequently, many individuals in the general population are diagnosed with thyroid nodules. However, no systematic review has focused on the prevalence of incidental thyroid nodules in asymptomatic adults or identified the

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Abbreviations

CI	Confidence Interval
I ²	Inconsistency Index
MHz	Megahertz
NOS	Newcastle–Ottawa Scale
OR	Odds Ratio
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	International Prospective Register of Systematic Reviews
ROB	Risk of Bias
US	Ultrasound
WHO	World Health Organization

associated factors. The aim of this systematic review and meta-analysis was to elucidate the prevalence of incidental thyroid nodules in asymptomatic adults and clarify the associated factors.

MATERIALS AND METHODS**Search strategies**

This scoping review has been registered with the Open Science Framework (<https://osf.io/mjb6v>). Reporting followed the PRISMA Extension for Scoping Reviews checklist. Two researchers (LJ and WL) independently searched the MEDLINE and Embase databases up to March 2024 to identify relevant articles. The following search terms were used: (“Nodule, Thyroid” OR “Nodules, Thyroid” OR “Thyroid Nodules”) AND (“Ultrasound”) AND (“Incidentaloma”). We limited the included studies to cross-sectional studies published in English. We also screened the reference lists of relevant studies

to identify additional eligible publications. The study selection process is shown in Figure 1.

Selection criteria

The inclusion criteria were asymptomatic adults and the use of US to examine the thyroid glands.

Data extraction

The following data were extracted by the authors (LJ and WL): basic information (first author name, year of publication, and location); participant characteristics (sample size, number of participants and incidentalomas, age, sex, frequency of US probes, and iodine status); and characteristics of the incidental thyroid nodules (size and nodularity).

Statistical analysis

We used R software with the “metaphor” package (version 4.6-0) and the “meta” package (version 7.0-0) for statistical calculations. We used logit and double arcsine transformations to calculate the prevalence with 95% confidence intervals (CIs) of incidental thyroid nodules for asymptomatic adults. In the subgroup analysis, the study population was divided by sex (male and female), age (older than 40–45 years and younger than 40–45 years), and frequency of US probes (<12 MHz was considered to be low frequency, more than 12 MHz was considered to be high frequency). We used the Cochran Q test and I^2 statistics to assess heterogeneity. When significant heterogeneity was found, a random effects model was used to pool the results; if heterogeneity was low, a fixed effects model was used to pool the results. Funnel plots were constructed to assess publication bias. We used a linear regression test of funnel plot asymmetry after arcsine transformations.

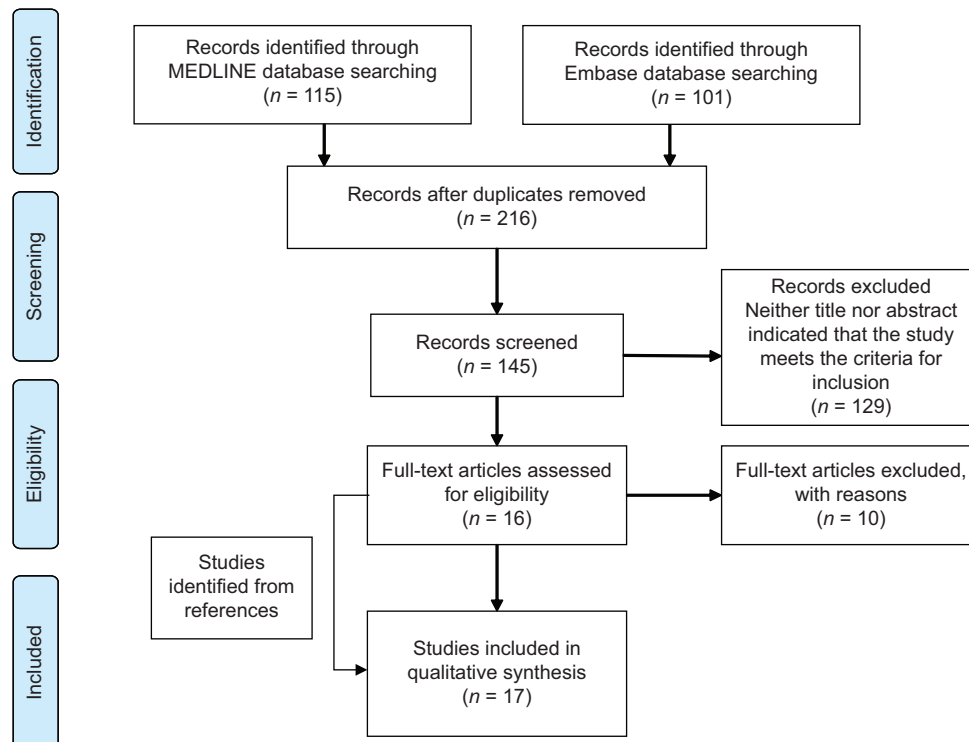
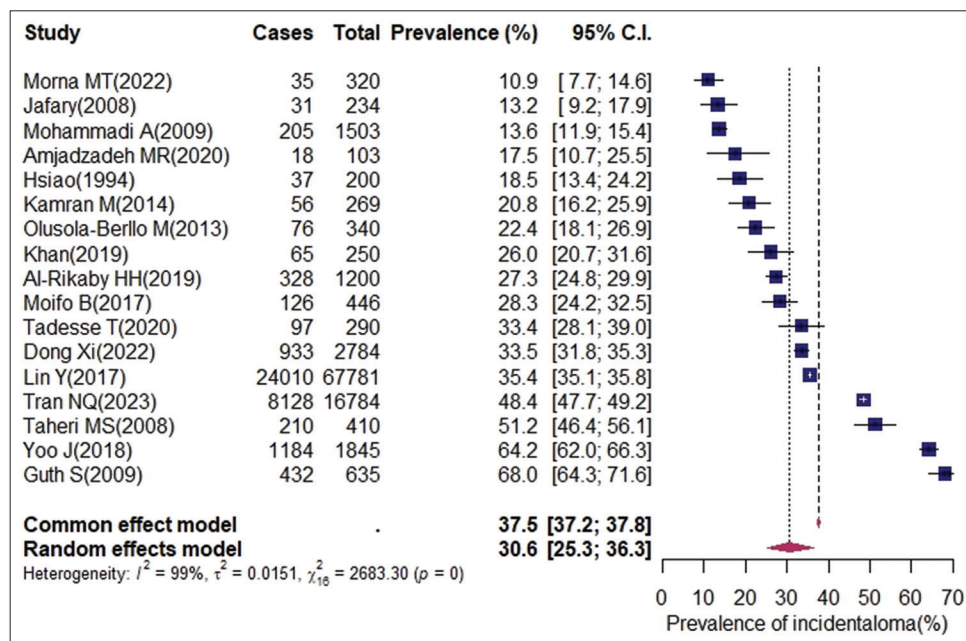


Figure 1: Flow chart showing the details of the study selection process

Table 1: Characteristics of the studies included in the review

Number	Author (year)	Country	Total number	Incidentaloma	Prevalence
1	Hsiao and Chang, 1994 ^[4]	Taiwan	200	37	18% (13%–25%)
2	Jafary <i>et al.</i> , 2008 ^[5]	Iran	234	31	13% (9%–18%)
3	Taheri, 2008 ^[6]	Iran	410	210	51% (46%–56%)
4	Mohammadi <i>et al.</i> , 2009 ^[7]	Iran	1503	205	14% (12%–15%)
5	Guth <i>et al.</i> , 2009 ^[8]	Germany	635	432	68% (64%–72%)
6	Olusola-Bello <i>et al.</i> , 2013 ^[9]	Nigeria	340	76	22% (18%–27%)
7	Kamran <i>et al.</i> , 2014 ^[10]	Pakistan	269	56	21% (16%–26%)
8	Moifo <i>et al.</i> , 2017 ^[11]	Cameroon	446	126	28% (24%–33%)
9	Liu <i>et al.</i> , 2017 ^[12]	China	67,781	24,010	35% (35%–36%)
10	Yoo <i>et al.</i> , 2018 ^[13]	Korea	1845	1184	64% (62%–66%)
11	Khan <i>et al.</i> , 2021 ^[14]	Pakistan	250	65	26% (21%–32%)
12	Al-Rikaby and Al-Subaiee, 2019 ^[15]	Iraq	1200	328	27% (25%–30%)
13	Amjadzadeh <i>et al.</i> , 2020 ^[16]	Iran	103	18	17% (11%–26%)
14	Tadesse <i>et al.</i> , 2020 ^[17]	Ethiopia	290	97	33% (28%–39%)
15	Morna <i>et al.</i> , 2022 ^[18]	Ghana	320	35	11% (8%–15%)
16	Dong <i>et al.</i> , 2022 ^[19]	China	2784	933	34% (32%–35%)
17	Tran <i>et al.</i> , 2023 ^[20]	Vietnam	16,784	8128	48% (48%–49%)
Total		<i>n</i> =17	95,394	35,971	30.6% (25%–36%)

**Figure 2:** Forest plot of the prevalence of thyroid incidentalomas identified with ultrasound; thyroid incidentalomas were detected by ultrasound in up to 30.6% of asymptomatic adults according to the random effects model

RESULTS

Characteristics of the included studies

Seventeen studies were ultimately included after searching the MEDLINE and Embase databases.^[4–20] A flow chart of the study selection process is shown in Figure 1, and the details of the included studies are summarized in Table 1. A total of 95,394 adults were enrolled, and 35,971 people were found to have incidentaloma through the US.

Meta-analysis results

The forest plot of the meta-analysis of incidentalomas is

shown in Figure 2. The prevalence of thyroid incidentaloma in this meta-analysis was 30.6% (95% CI: 26.3–36.3, $I^2 = 99\%$, $P < 0.01$). Due to significant heterogeneity, we used a random effects model to estimate the prevalence.

According to the subgroup analysis [Table 2], the prevalence rates of thyroid incidentaloma were 34% (95% CI: 27–42, $I^2 = 99\%$, $P < 0.01$) and 23% (15%–32% $I^2 = 99\%$, $P < 0.01$) for females and males, respectively. The prevalence rates of thyroid incidentaloma were 42% (95% CI: 30–54, $I^2 = 99\%$, $P < 0.01$) and 20% (12%–29% $I^2 = 99\%$, $P < 0.01$) for individuals aged more than 50–55 and <50–55 years, respectively. The

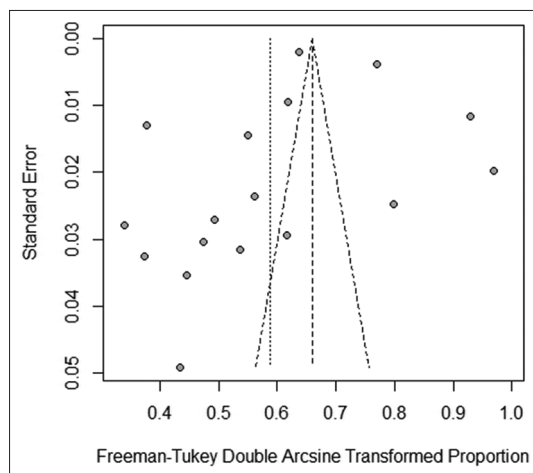
Table 2: Prevalence of thyroid incidentaloma identified through ultrasound and subgroup analysis

Category	Prevalence (95% CI)
General population	30.6% (25.3%–36.3%)
Gender	
Female	34% (27%–42%)
Male	23% (15%–32%)
Age (years)	
Age more than 50–55	42% (30%–54%)
Age <50–55	20% (12%–29%)
US probe	
Low-frequency US	25% (19%–31%)
High-frequency US	60% (48%–72%)

CI: Confidence interval, US: Ultrasound

Table 3: The distribution of nodule size and nodularity among thyroid incidentalomas identified with ultrasound

Variables	Percentage
Nodule (cm)	
Size <1	70 (61–78)
Size >1	30 (22–39)
Nodularity	
Single	59 (49–68)
Multiple	41 (32–52)

**Figure 3:** A funnel plot was constructed to assess publication bias, and there was no significant publication bias ($P = 0.58$)

prevalence rates of thyroid incidentaloma were 60% (95% CI: 48–72, $I^2 = 99\%$, $P < 0.01$) and 25% (95% CI: 19%–31%, $I^2 = 99\%$, $P < 0.01$) for the high-frequency (>12 MHz) and low-frequency US groups, respectively.

The majority of thyroid incidentalomas were smaller than one centimeter (70%, 95% CI 61%–78%, $I^2 = 99\%$, $P < 0.01$) and had singular nodules (59%, 95% CI: 49%–68%, $I^2 = 99\%$, $P < 0.01$) [Table 3]. According to the funnel plot analysis, there was no significant publication bias in the included publications ($P = 0.58$) [Figure 3].

DISCUSSION

This is the first systematic review and meta-analysis of asymptomatic thyroid nodules identified by the US. According to the results, up to 30% of asymptomatic adults will have thyroid incidentalomas detected by the US. There was a higher prevalence of thyroid incidentalomas among women, older people, and those who underwent higher-frequency US. Most incidentalomas are single nodules (59%) and are smaller than one centimeter (70%) in size.

The global incidence of thyroid cancer has been increasing.^[21] However, the mortality rate has not changed. This phenomenon is indicative of overdiagnosis and overtreatment,^[22] which could be associated with the widespread use of routine cancer screening, especially in South Korea and other countries.^[2] After changing the guidelines for thyroid nodule examination in Korea, the prevalence of this disease decreased.^[23] In Taiwan, we also have an overdiagnosis of early and low-risk thyroid cancer.^[3]

To date, there is still no consensus regarding recommendations for thyroid cancer screening. According to the American Thyroid Association guidelines^[24] and Korea guidelines,^[25] there is insufficient evidence to recommend routine screening for thyroid cancers. Among thyroid incidentaloma identified by the US, up to 28.8% of cases were reported as cancer.^[26] The screening of thyroid cancer lesions has led to the early diagnosis of thyroid cancer. On the other hand, according to autopsy data, an average of 10% of people who died without thyroid disease had small thyroid cancer.^[27] This means that small thyroid cancers are indolent and that routine screening and treatment of early-stage papillary thyroid cancer can lead to overdiagnosis and overtreatment. Recently, a meta-analysis of thyroid screening data revealed a survival benefit of screening compared to symptomatic thyroid cancer. Indeed, some screening-identified cancers are at an advanced stage, and early treatment can lead to benefits.^[28]

Professor Miyauchi proposed an active surveillance program for subcentimeter low-risk thyroid papillary cancer in 1993.^[29] Most patients can be under surveillance, and there is no need for surgery. Delaying surgery provides the same survival rate. According to our studies, most thyroid incidentalomas are also subcentimeter in size. Therefore, screening for thyroid cancer is still controversial. Clinicians should ensure an adequate diagnosis of early-stage thyroid cancer and provide appropriate treatment to avoid overtreatment.

We also noted that several factors are associated with a greater incidence of thyroid cancer, such as female sex,^[30] age,^[31] and the use of more high-frequency probes. These findings are comparable to those of previous reports. Some studies also reported more thyroid nodules in patients with metabolic syndrome.^[30]

There are several limitations in this review. First, not all of the included studies reported the status of iodine deficiency or radiation exposure; therefore, we cannot estimate the effect of iodine deficiency or radiation exposure on thyroid nodules. Second, the number of enrolled studies was small, and there was significant heterogeneity. These results may not represent the real incidence worldwide. Third, the malignancy rates of these thyroid incidentalomas were not reported in the included studies due to the cross-sectional study design. Fourth, while we conducted a systematic review, we recognize the concentration of references from certain countries, such as Iran and Korea. This may limit the generalizability of our findings, as these regions may have unique characteristics that are not representative of other populations. Fifth, our study focused only on asymptomatic thyroid incidentalomas; however, some studies included both palpable and nonpalpable nodules. In these studies, which included asymptomatic but palpable patients, the incidence of incidental tumors may have been overestimated.

CONCLUSION

With the frequent use of the US, a large number of thyroid incidentalomas can be discovered in asymptomatic individuals. Up to 30% of asymptomatic adults have thyroid incidentalomas detected by the US. Thyroid incidentalomas are more common in women, elderly people, and people with higher US frequencies. Most incidentalomas are solitary and <1 cm in size. Clinicians should pay attention to this phenomenon and avoid overdiagnosis and overtreatment.

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Conflicts of interest

There are no conflicts of interest.

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