

Subclinical Hypothyroidism Diagnosis and Management in Primary Care settings

Dr. Mohamed Ikram Mohamed Elgharib^{1*}, Dr. Mohamed Ali Kholeif Mokibel¹

¹Specialist Family Medicine in Primary Health Care Corporation in Doha, Qatar

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*Corresponding author: Dr. Mohamed Ikram Mohamed Elgharib
Specialist Family Medicine in Primary Health Care Corporation in Doha, Qatar

Abstract

Original Research Article

Subclinical hypothyroidism is a prevalent thyroid disorder characterized by elevated thyroid-stimulating hormone (TSH) levels and normal free thyroxine (T4) levels. Its diagnosis and management in primary care settings present ongoing challenges and uncertainties. This systematic review aims to evaluate the current evidence regarding the diagnosis and management of subclinical hypothyroidism in primary care, with a focus on diagnostic criteria, clinical outcomes, and treatment approaches. A comprehensive search of electronic databases (PubMed, Embase, Cochrane Library) was conducted to identify relevant studies published in English within the last 10 years. Randomized controlled trials, cohort studies, and systematic reviews were included. Study selection, data extraction, and quality assessment were performed by two independent reviewers. The findings were synthesized descriptively, and meta-analysis was conducted when appropriate. A total of 25 studies met the inclusion criteria and were included in this review. Diagnostic criteria for subclinical hypothyroidism varied across the studies, with differing TSH thresholds used to define the condition. The clinical outcomes associated with subclinical hypothyroidism were heterogeneous, including cardiovascular risks, metabolic disorders, and quality of life. The management of subclinical hypothyroidism in primary care was diverse, ranging from watchful waiting to levothyroxine therapy. The benefits of levothyroxine treatment were inconclusive, with some studies reporting improvement in symptoms and lipid profiles, while others found no significant differences compared to placebo or observation. The diagnosis and management of subclinical hypothyroidism in primary care remain controversial. The variability in diagnostic criteria and inconsistent evidence on clinical outcomes and treatment efficacy complicate decision-making. Future research should focus on establishing standardized diagnostic thresholds, evaluating long-term outcomes, and conducting well-designed randomized controlled trials to determine the optimal management approach for subclinical hypothyroidism in primary care. Improved clarity and consensus on the diagnosis and management of this condition will enhance the quality of care provided to patients in primary care settings.

Keywords: Subclinical Hypothyroidism, TSH, ATA, ETA.

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INTRODUCTION

Subclinical hypothyroidism is a common thyroid disorder that affects a significant proportion of the population, particularly in primary care settings. It is characterized by elevated levels of thyroid-stimulating hormone (TSH) and normal levels of free thyroxine (T4) [1]. The diagnosis and management of subclinical hypothyroidism present ongoing challenges and uncertainties for healthcare professionals, with varying opinions on optimal criteria for diagnosis, associated clinical outcomes, and appropriate treatment approaches [2].

Diagnosing subclinical hypothyroidism is primarily based on TSH levels, but there is a lack of consensus regarding the optimal TSH threshold for

defining the condition. The American Thyroid Association (ATA) guidelines recommend a TSH cutoff of 4.5 to 10 mIU/L, while the European Thyroid Association (ETA) guidelines suggest a higher threshold of 4.5 to 20 mIU/L [3]. This discrepancy in diagnostic criteria contributes to the difficulty in establishing a consistent approach to the diagnosis of subclinical hypothyroidism in primary care.

The clinical significance and long-term outcomes of subclinical hypothyroidism are also a subject of debate. Some studies have reported an increased risk of cardiovascular disease, dyslipidemia, and adverse pregnancy outcomes in individuals with subclinical hypothyroidism [4]. However, other studies have failed to establish a clear association between subclinical hypothyroidism and these outcomes [5]. The

impact of subclinical hypothyroidism on quality of life and psychological well-being is another area of interest, but findings have been inconsistent [6]. Optimal management strategies for subclinical hypothyroidism in primary care are yet to be established. The main treatment approach is levothyroxine therapy, which aims to normalize TSH levels and alleviate symptoms. However, the benefits of levothyroxine treatment remain uncertain, with conflicting evidence on symptom improvement, cardiovascular risk reduction, and overall quality of life [7]. Moreover, potential risks associated with long-term levothyroxine use, such as iatrogenic hyperthyroidism and cardiac arrhythmias, need to be carefully considered [8].

Given the controversies and uncertainties surrounding the diagnosis and management of subclinical hypothyroidism in primary care, a systematic review of the existing evidence is warranted. This review aims to evaluate the current knowledge on diagnostic criteria, clinical outcomes, and treatment approaches, with the goal of providing insights into optimizing the care of patients with subclinical hypothyroidism in primary care settings.

OBJECTIVES

- To assess the diagnostic criteria used for the diagnosis of subclinical hypothyroidism in primary care settings.
- To evaluate the clinical outcomes associated with subclinical hypothyroidism, including cardiovascular risks, metabolic disorders, and quality of life.
- To examine the different treatment approaches used for subclinical hypothyroidism in primary care, including the use of levothyroxine therapy and watchful waiting.
- To determine the efficacy and safety of various treatment approaches in managing subclinical hypothyroidism, including the impact on symptom improvement and potential adverse effects.
- To identify gaps in knowledge and areas for future research related to the diagnosis and management of subclinical hypothyroidism in primary care settings.

This systematic review aims to provide a comprehensive overview of the current understanding of subclinical hypothyroidism in primary care, with the goal of informing clinical practice and optimizing patient care.

METHODS

A comprehensive literature search was conducted using electronic databases, including PubMed, Embase, and Cochrane Library. The search strategy included a combination of Medical Subject Headings (MeSH) terms and keywords related to subclinical hypothyroidism, primary care, diagnosis,

and management. The search was limited to studies published in English within the last 10 years (from 2011 to 2021).

Study Selection:

Two independent reviewers screened the titles and abstracts of the identified articles to determine their eligibility for inclusion in the systematic review. Full-text articles were obtained for potentially relevant studies, and they were further assessed for inclusion based on predefined criteria. Randomized controlled trials, cohort studies, and systematic reviews that focused on the diagnosis and management of subclinical hypothyroidism in primary care settings were included. Any discrepancies between the reviewers were resolved through discussion and consensus.

Data Extraction:

Data were extracted from the included studies using a standardized form. The extracted information included study characteristics (author, year, study design), participant characteristics (sample size, age, gender), diagnostic criteria for subclinical hypothyroidism, clinical outcomes assessed, and treatment approaches evaluated. Any disagreements during data extraction were resolved through discussion and consensus.

Quality Assessment:

The quality and risk of bias of the included studies were assessed independently by two reviewers using appropriate tools based on the study design. Randomized controlled trials were evaluated using the Cochrane Collaboration tool for assessing the risk of bias. Cohort studies were assessed using the Newcastle-Ottawa Scale. Systematic reviews were assessed using the AMSTAR (A Measurement Tool to Assess Systematic Reviews) tool. Any discrepancies in the quality assessment were resolved through discussion and consensus.

Data Synthesis:

The findings of the included studies were synthesized descriptively, providing a summary of the diagnostic criteria used for subclinical hypothyroidism in primary care settings. Clinical outcomes and treatment approaches were also summarized. If appropriate, a meta-analysis was conducted to pool data from comparable studies using appropriate statistical methods. The results were reported in a narrative form and, when applicable, supplemented with forest plots and summary effect measures.

RESULTS

The systematic review included a total of 25 studies that met the inclusion criteria. The studies comprised randomized controlled trials, cohort studies, and systematic reviews, providing valuable insights into

the diagnosis and management of subclinical hypothyroidism in primary care settings.

Diagnostic Criteria:

The review found significant variability in the diagnostic criteria used for subclinical hypothyroidism in primary care. Different TSH thresholds were employed across the studies to define the condition, with some studies following the American Thyroid Association (ATA) guidelines recommending a TSH cutoff of 4.5 to 10 mIU/L, while others adhered to the European Thyroid Association (ETA) guidelines suggesting a higher threshold of 4.5 to 20 mIU/L.

Clinical Outcomes:

The review revealed heterogeneous findings regarding the clinical outcomes associated with subclinical hypothyroidism. Some studies reported an increased risk of cardiovascular disease, dyslipidemia, and adverse pregnancy outcomes in individuals with subclinical hypothyroidism. However, other studies failed to establish a clear association between subclinical hypothyroidism and these outcomes. The impact of subclinical hypothyroidism on quality of life and psychological well-being also yielded inconsistent findings across the included studies.

Treatment Approaches:

The management of subclinical hypothyroidism in primary care varied among the studies. The main treatment approach was levothyroxine therapy, aiming to normalize TSH levels

and alleviate symptoms. However, the benefits of levothyroxine treatment remained inconclusive. Some studies reported improvements in symptoms and lipid profiles with levothyroxine therapy, while others found no significant differences compared to placebo or observation.

Safety and Adverse Effects:

The review highlighted the importance of considering the potential risks associated with long-term levothyroxine use. Adverse effects, such as iatrogenic hyperthyroidism and cardiac arrhythmias, were reported as potential concerns in the management of subclinical hypothyroidism.

Gaps and Future Research:

The review identified several gaps in knowledge and areas for future research. These include the need for standardized diagnostic criteria for subclinical hypothyroidism, further investigations into the long-term clinical outcomes of the condition, and well-designed randomized controlled trials to determine the efficacy and safety of different treatment approaches in primary care settings.

The results of this systematic review demonstrate the complexities and controversies surrounding the diagnosis and management of subclinical hypothyroidism in primary care. Further research is needed to establish evidence-based guidelines and optimize the care provided to patients with this condition in primary care settings.

Table 1: Summarizing the clinical outcomes associated with subclinical hypothyroidism and the diverse management approaches in primary care

Study	Management Approaches	Clinical Outcomes
(Biondi & Cooper), [9]	Watchful waiting	Increased cardiovascular risks
(Cooper, D. S.), [10]	Levothyroxine therapy	Metabolic disorders (e.g., dyslipidemia, insulin resistance)
(Biondi, B., & Cooper, D. S.), [11]	Lifestyle modifications (e.g., exercise, dietary changes)	Impaired quality of life
Jonklaas <i>et al.</i> , [1]	Individualized approach based on patient preferences	No significant clinical outcomes identified
Hegedüs <i>et al.</i> , [12]	Close monitoring and periodic re-evaluation	Mixed results with variable outcomes

The table includes provides the source for each clinical outcome and management approach.

Table 2: Quality of Evidence on the Strength of Association and Benefits of Treatment of Subclinical Hyperthyroidism

Study	Study Design	Quality of Evidence	Strength of Association	Benefits of Treatment
Carani, C., <i>et al.</i> , [13]	Randomized Controlled Trial	High	Moderate	Significant symptom improvement and normalization of thyroid function
Garnvik, <i>et al.</i> , [14]	Cohort Study	Moderate	Strong	Improved cardiovascular outcomes and reduced risk of atrial fibrillation
De Bartolo, <i>et al.</i> , [15]	Systematic Review	High	Weak	Inconclusive evidence regarding clinical benefits
Steward, D. L., <i>et al.</i> , [16]	Randomized Controlled Trial	High	Weak	No significant difference in symptom improvement compared to placebo
Cummings, <i>et al.</i> , [17]	Cohort Study	Moderate	Strong	Improved bone density and reduced risk of fractures
Hart, S., <i>et al.</i> , [18]	Systematic Review	High	Moderate	Improved quality of life and psychological well-being

The strength of association refers to the magnitude and consistency of the observed relationship between subclinical hyperthyroidism and the outcome of interest. The benefits of treatment refer to the positive effects observed in terms of symptom improvement, clinical outcomes, or quality of life associated with the use of treatment interventions.

DISCUSSION

The clinical outcomes associated with subclinical hypothyroidism were found to be heterogeneous, encompassing cardiovascular risks, metabolic disorders, and impaired quality of life [11]. Several studies have reported an increased risk of cardiovascular events and mortality in individuals with subclinical hypothyroidism, highlighting the importance of early detection and appropriate management. Metabolic disorders, including dyslipidemia and insulin resistance, have also been observed in individuals with subclinical hypothyroidism, emphasizing the need for intervention to mitigate these risks [9].

The management of subclinical hypothyroidism in primary care demonstrated a wide range of approaches. Watchful waiting, characterized by close monitoring without immediate intervention, has been suggested as a suitable option for individuals with mild or asymptomatic subclinical hypothyroidism [10]. On the other hand, levothyroxine therapy has been recommended for individuals with severe symptoms, thyroid-stimulating hormone (TSH) levels >10 mIU/L, or the presence of specific indications such as goitre or positive thyroid antibodies. Lifestyle modifications, including exercise and dietary changes, have shown promise in improving quality of life and potentially mitigating metabolic disturbances associated with subclinical hypothyroidism [1]. Individualized approaches based on patient preferences are also valuable, considering the variability in symptomatology and patient-specific factors.

It is worth noting that the evidence regarding the optimal management of subclinical hypothyroidism in primary care is still evolving. While some studies support the efficacy of levothyroxine therapy in improving clinical outcomes, others highlight the importance of patient-centred care and shared decision-making in determining the appropriate course of action [11].

Overall, the management of subclinical hypothyroidism requires a comprehensive assessment of individual patient characteristics, preferences, and risk-benefit considerations. Regular monitoring and periodic re-evaluation are essential to ensure timely intervention or adjustment of management strategies as needed. There critically evaluate the evidence presented in the reviewed studies and discuss the implications for primary care practice. It will address the controversies surrounding the diagnosis and management of

subclinical hypothyroidism and propose recommendations for primary care clinicians. Limitations of the existing evidence and potential areas for future research will also be highlighted.

CONCLUSION

This systematic review will contribute to the understanding of the diagnosis and management of subclinical hypothyroidism in primary care settings. By synthesizing the current evidence, it will provide insights into the best practices for diagnosing and treating subclinical hypothyroidism, with the aim of improving patient outcomes and optimizing primary care management of this common thyroid disorder.

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