

REVIEW

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Thyroid disorders in patients with human immunodeficiency virus infection: a meta-analysis

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Abstract

Background Thyroid disorders have significant clinical sequelae, including impaired growth in children, metabolic abnormalities, and impaired cognitive function. However, available studies on burden of thyroid diseases in people with human immunodeficiency virus (HIV), particularly its prevalence and its interaction with HIV related factors (like CD4 count), are controversial. This review aimed to provide a comprehensive summary and analysis on the extent of thyroid dysfunctions in this population.

Methods Following Preferred reporting items for systematic review and meta-analysis (PRISMA) guidelines, a comprehensive search was done through Medline/PubMed, Web of Science, Science Direct, and World Health Organization Virtual Health Library Regional Portal. Using Comprehensive Meta-Analysis Software version 3.3, we calculated the pooled prevalence and standardized mean difference (SMD) estimates with 95% confidence intervals (CIs).

Results A total of 30 studies met the eligibility criteria and were further included for the analyses. The most common types of thyroid dysfunction identified among HIV patients were subclinical hypothyroidism (7.7%), overt hypothyroidism (2.7%), sick euthyroid syndrome (2.47%), isolated low FT4 (1.80%), and overt hyperthyroidism (0.7%). Hypothyroidism among HIV patients was significantly associated with lower CD4 count ($p < 0.001$). The analysis revealed that only FT4 levels had significant differences between patients with HIV and healthy people ($p = 0.013$).

Conclusion Individuals with HIV are at risk of developing variable manifestations of thyroid abnormalities. While being not abundant in the HIV population, monitoring of thyroid dysfunction is essential due to the potential for progression to overt hypothyroidism and associated adverse health outcomes.

Keywords Thyroid, Thyroid disorders, Hypothyroidism, Prevalence, Human immunodeficiency virus, HIV

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Background

Human immunodeficiency virus (HIV) infection is a condition characterized by decreased CD4 cell count and immunodeficiency, leading to increased risk of developing a variety of opportunistic infections and tumors [1, 2]. Globally, it has estimated that 38 million people were living with HIV in 2019, including 1.8 million children [3]. In addition, it has estimated that near 1.7 million people newly infected with HIV/AIDS and 690,000 people dying from HIV infection and acquired immunodeficiency syndrome (AIDS)-related diseases [3]. Patients with HIV can survive longer due to the use of highly active antiretroviral therapy (HAART). Due to this mortality reduction, HIV infection has transformed into a manageable chronic illness. At the same time, with a prolonged life expectancy, patients with HIV face challenges of co-occurring chronic conditions or comorbidities [4, 5].

Growing evidence suggests a significant interplay between HIV and endocrine dysfunction like insulin resistance and dyslipidemia, which have garnered increasing attention due to its potential impact on the long-term overall health and quality of life [5, 6]. Among the various endocrine abnormalities observed in HIV patients, thyroid dysfunction and alterations in thyroid hormones levels have been described in HIV patients [7–9]. In addition to overt or clinical thyroid diseases, other thyroid disorders have been described in patients with HIV such as subclinical thyroid diseases, isolated low free thyroxine (FT4) levels, and non-thyroidal illness, also known as euthyroid sick syndrome [10].

Thyroid-stimulating hormone (TSH), which is a sensitive marker of thyroid condition, stimulates thyroid cell growth and function through its receptor, causing release of thyroid hormones thyroxine (T4) and triiodothyronine (T3) that regulate cell growth, brain development, and energy metabolism, and thyroid hormones unbound to thyroxine-binding globulin in serum are identified as free T3 (FT3) and FT4 [11–14]. Hypothyroidism occurs when TSH concentrations in serum are above the normal range with T4 levels below the normal range, while hyperthyroidism is defined as falling of TSH levels below the normal range with high T4 levels [11]. Subclinical hypothyroidism is characterized by mildly elevated TSH level (5–10 mIU/L) and normal FT4 [15].

The prevalence of thyroid diseases following HIV infection is reported differently in various studies. However, there have been controversies on the influence of HIV on thyroid functioning. While recognition of several endocrine abnormalities is critical for optimal patient care, there is a disparity in the available data about the burden of thyroid abnormalities in people with HIV, particularly its prevalence and its interaction with HIV related factors like CD4 count and use of HAART. This review aimed

to provide systematic analyses and summary of the current evidence and identify areas where further research is needed in order to improve the medical care of individuals living with HIV.

Methods

Search approach and studies inclusion criteria

The methodology for this review adhered to the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [16]. This review was registered previously on Open Science Framework platform (<https://osf.io/ew3a4/>). The systematic search covered all available literature from its inception up to July 2024. The PEO framework was used to clarify the aim of this research. Accordingly, population (HIV patients), exposure (HIV), and outcome (different types of thyroid disorders such as hypothyroidism and sub clinical hypothyroidism) was used for this review. In addition to estimating prevalence rates of thyroid disorders, we aimed to assess the level of thyroid function by comparing differences in thyroid hormones levels among patients with HIV and healthy people who were included in the studies as controls.

To gather relevant literature, we conducted a systematic literature search using the electronic databases of PubMed, Web of Science, ScienceDirect, and World Health Organization Virtual health library Regional Portal. There were no restrictions applied to the search in terms of sex, race, geographical area, or publication date. Details of the search terms were included in (Supplementary material. 1). We reviewed the articles referenced by the included articles to ensure no possible relevant articles were missed. The publications that were found were uploaded to Endnote software to expedite initial screening of titles and abstracts and remove detect duplicate entries.

Inclusion and exclusion criteria

The selection process involved a two-step approach. Initially, we screened the titles and abstracts of all identified articles to identify potentially relevant studies. Subsequently, we conducted a comprehensive full-text review of these selected studies to assess their eligibility based on the predefined inclusion criteria.

The inclusion criteria for the articles in this review included cross-sectional, case-control, or cohort studies that provided explicit data on the number of patients with HIV both with and without thyroid abnormalities. Additionally, we included studies that provided data on thyroid-stimulating hormone (TSH), triiodothyronine (T3), thyroxine (T4), free T3 (FT3), and free T4 (FT4) levels in both HIV patients and their healthy control groups. We excluded case reports, editorials, reviews,

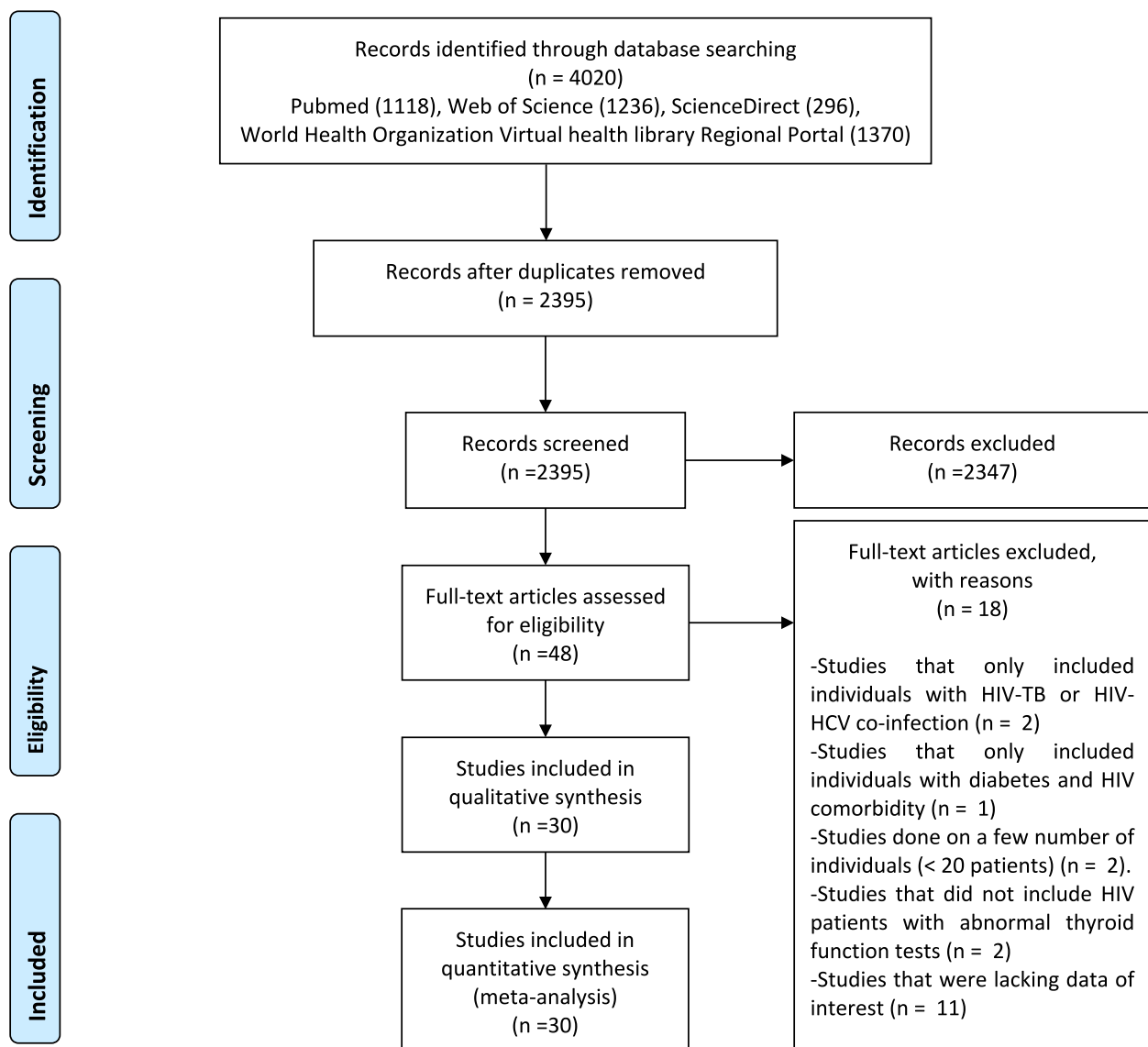


Fig. 1 Flow chart for studies selection process

abstracts, and studies that did not provide sufficient data on the variables of interest.

Quality assessment and data extraction

To evaluate the methodological rigor and potential biases in the included studies, we employed the critical appraisal checklists provided by the Joanna Briggs Institute (<https://jbi.global/critical-appraisal-tools>). These checklists facilitate assessment of the possibility of bias in study design, conduct, and data analysis. The data extraction process involved four independent reviewer for extracting relevant information from each study. Any discrepancies or inconsistencies among the reviewers were

resolved through thorough discussion and consensus. The data extracted from the each study included author, year, region, number of patients, age group of the participants, number of HIV patients with thyroid diseases, and the levels of serum TSH, T3, T4, FT3, and FT4. In addition, we summarized data on any significant associations with lipid profile abnormalities. Furthermore, we summarized data on any underlying contributing factors for developing thyroid abnormalities among HIV patients, if available.

Table 1 Baseline characteristics of the studies included in the review:

Study	Country	Age group	No. of HIV Patients	Quality assessment	Factors associated with hypothyroidism or other findings
Akinsete et al. [21]	Nigeria	Children mean age 9.23 ± 4.06 years	83	8/8	FT3 was correlated with CD4 count and viral load. No association between the types of HAART used and thyroid abnormalities
Beltran et al. [22]	France	Adults 41.3 ± 10.4 years	343	6/8	Hypothyroidism was correlated with Stavudine and low CD4 cell count
Bongiovanni et al. [23]	Italy	Adults 38 (23–66) years	190	8/8	In the multivariable analysis, higher total cholesterol levels was the only factor significantly associated with subclinical hypothyroidism. HAART was not associated with thyroid dysfunction
Carvalho et al. [24]	Brazil	Adults 46.5 ± 9.1 years	153	7/8	HAART was associated with thyroid dysfunction
Dev et al. [25]	India	Adults 36.6 ± 10.2 years	225	8/8	Positive correlation between FT3 and FT4 with CD4 cell count. Negative correlation between TSH and CD4 cell count
Dutta et al. [26]	India	Adults 35.85 ± 8.89 years	95	5/8	Thyroid dysfunctions were more common in females and in those with low CD4 cell count. However, no statistical test of significance was conducted
Emokpae et al. [27]	Nigeria	Adults	200	6/10	Significant correlation between and CD4 cell count and T4. HAART was associated with TSH, T3, and T4. HAART was not associated with Sub-clinical hypothyroidism
Gangannavar et al. [29]	India	Adults	300	6/8	Thyroid dysfunction was significantly more frequent in the HAART. The mean CD4 count was significantly lower in patients with hypothyroidism than in the other patients
Hatzl et al. [31]	Austria	Adults 10–74 years	410	6/8	NRTI intake was correlated with elevated TSH in HIV patients. No association with NNRTIs, PIs, or low CD4 count
Harsløf et al. [30]	Denmark	Adults 51 ± 11 years	826	6/8	Thyroid dysfunction was not associated with HIV infection or CD4 count
Jain et al. [32]	India	Adults 34.10 ± 8.3 years	100	6/8	Thyroid dysfunction was not associated CD4 count
Ji et al. [33]	China	Adults 48.72 ± 10.92	178	8/8	The mean CD4 count was significantly lower in patients with hypothyroidism than in the other patients. Thyroid dysfunction is more common in HIV patients on HAART than in the HAART-naïve group, mainly manifested as hypothyroidism FT3/FT4 levels were negatively related to HIV duration and FT3 levels were positively related to CD4 cell
Kaneria et al. [34]	India	Adults 30–50 years	75	6/8	As the stage of HIV advanced, the FT3 and FT4 levels went on decreasing. TSH levels did not correlate with the stage of infection Inverse correlation between TSH levels and CD4 counts. The mean TSH levels in patients on HAART were significantly higher than in patients not on HAART. Cryptococcal meningitis was found to be associated with subclinical hypothyroidism, CNS toxoplasmosis with isolated low FT4 levels and tuberculosis with sick euthyroidism
Ketsamathi et al. 2006	Thailand	Adults 36.3 ± 8.3 years	200	8/8	Hypothyroidism was not significantly associated with CD4 count or HAART
Kotwal et al. [50]	India	Adults 37.19 ± 8.79 years	100	7/8	n/a
Madeddu et al. [37]	Italy	Adults 20–62 years	202	9/11	Subclinical hypothyroidism was associated with HAART (particularly Stavudine)

Table 1 (continued)

Study	Country	Age group	No. of HIV Patients	Quality assessment	Factors associated with hypothyroidism or other findings
Madge et al. [38]	UK	Adults Median age 37 years	1565	7/8	No independent variables were significantly associated with overt hypothyroidism, including HAART
Noureldeen et al. [39]	Saudi Arabia	Adults 22–47 years	100	7/10	Most of HIV-infected patients had normal values of thyroid autoantibodies
Omolumen et al. 2024	Nigeria	Adults 39.34 ± 11.76 years	80	5/8	HIV-infected patients had higher TSH and lower T3 and T4 than normal participants
Olivieri et al. [40]	Italy	Adults aged 24–55	119	6/10	HIV-infected patients had lower FT4 levels and higher TSH and TBG values than euthyroid normal controls
Porwal et al. [41]	India	Adults Mean age 38.84 years	70	7/9	No significant correlation between TSH and free T4 level and CD4 count
Properzi et al. [42]	Italy	Adults 46.6 ± 11.5 years	6343	7/9	hypothyroidism was associated with older age, female sex, and low CD4 count
Sebastian et al. [43]	India	Adults 43.3 ± 10	159	6/8	Inverse correlation between TSH and CD4 counts. No association between thyroid dysfunction and HAART
Sharma et al. [44]	India	18–70 years	359	8/8	Subclinical hypothyroidism was associated with low CD4 count
Silva et al. [45]	Brazil	43.69 ± 1.06 years	117	6/8	Significant association of risk between Stavudine and subclinical hypothyroidism
Thongam et al. [46]	India	Children under 13 years	60	7/8	Inverse correlation between TSH and CD4 counts
Tripathy et al. [47]	India	Adults 37.88 ± 7.8 year	43	7/8	No correlation between serum hormone levels and CD4 count
Verma et al. [48]	India	Adults 20–80 years	100	8/8	Inverse correlation between TSH and CD4 counts
Vigano et al. [49]	US	Children	52	8/8	Patients with low FT4 values as compared with children without thyroid dysfunction showed lower CD4+ count and lower duration of HAART exposure
Ukodei et al. 2023	Nigeria	Majority 31–40 years	95	8/8	TSH and ft3 were significantly higher in patients on HAART than in the control and the HIV positive not on HAART

Statistical analysis

The statistical analyses were carried out by using Comprehensive Meta-Analysis Software version 3.3 (Biostat, Englewood, NJ, USA; <http://www.Meta-Analysis.com>) to calculate the pooled summary prevalence and standardized mean difference (SMD). Random-effects model was used to compensate for the heterogeneity of studies. Heterogeneity among studies was evaluated using the I^2 statistic, which quantifies the percentage of variation in effect estimates attributable to heterogeneity rather than chance. Publication bias, a potential source of bias due to the tendency for studies with statistically significant results to be published more often, was assessed using Begg's and Egger's tests. Funnel plots were visually inspected to assess publication bias if the number of studies exceeded 10 [17–19]. When publication bias was detected, the Duval and Tweedie trim-and-fill method

was applied to adjust for potentially missing studies [20]. The significance level for all analyses was set at 0.05.

Results

Studies characteristics

The schematic flow of the study identification and selection process is presented in Fig. 1. Initially, the search yielded a total of 4020 records. After removing duplicate data, 2395 studies were included for the title and abstract screening. Of which, 2347 were excluded due to irrelevance. The full texts of the remaining 48 records were screened, and 18 records were excluded for specific reasons: studies that only included individuals with HIV/TB or HIV/HCV co-infection ($n=2$), studies focusing solely on individuals with diabetes mellitus and HIV comorbidity ($n=1$), studies conducted on a small number of individuals (<20 patients) ($n=2$), studies that excluded HIV patients with abnormal thyroid function tests ($n=2$), and

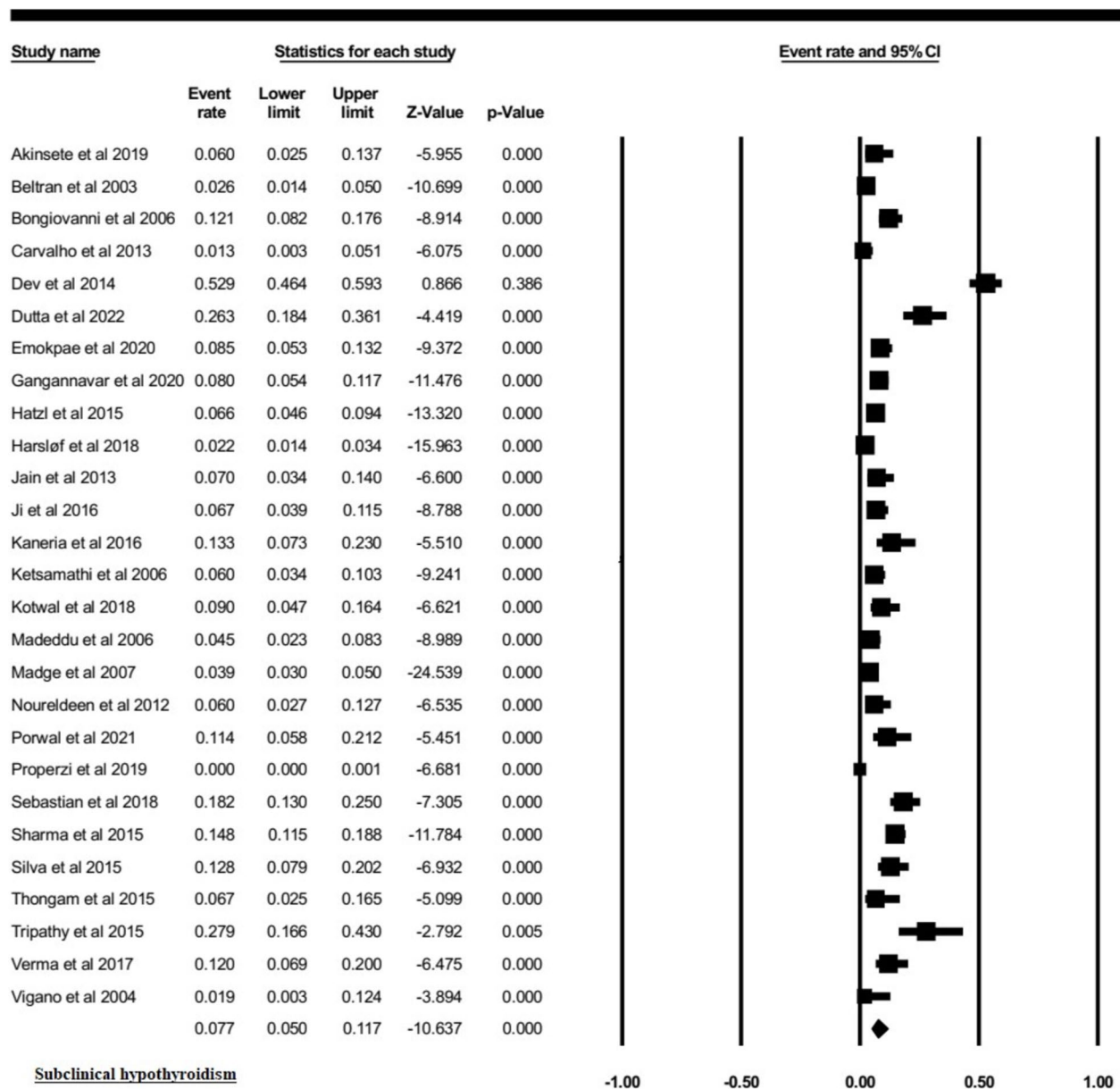
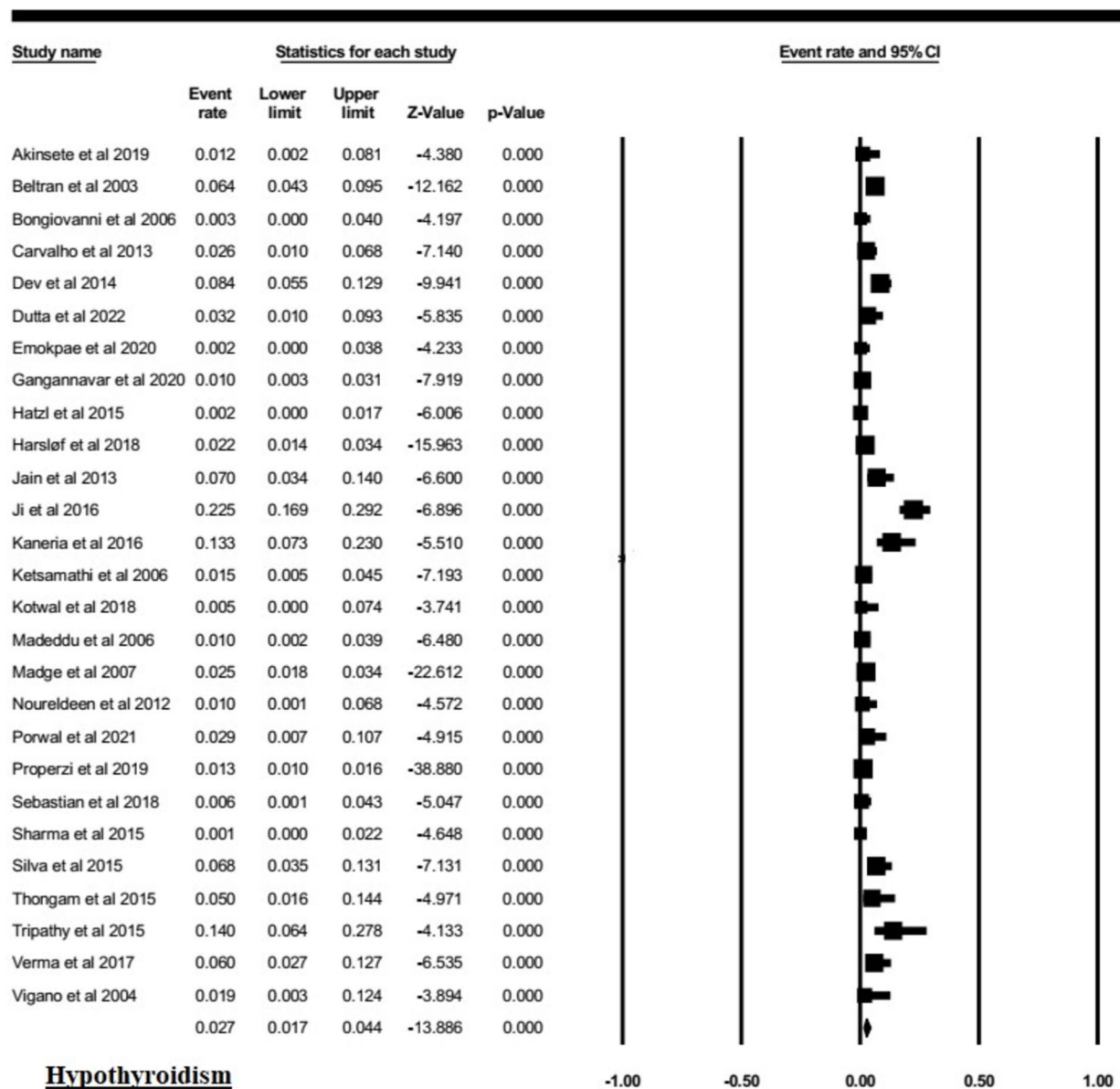


Fig. 2 Pooled prevalence of subclinical hypothyroidism in patients with HIV

studies lacking data of interest ($n=11$). Lastly, a total of 30 studies met the eligibility criteria and were further included for evidence synthesis [21–50]. The main features of the included studies, including risk of bias assessment, are presented in Table 1.

The most common types of thyroid dysfunction identified in the studies included among individuals with HIV were subclinical hypothyroidism, overt hypothyroidism, sick euthyroid syndrome, isolated low FT4, and overt hyperthyroidism. Some studies reported data on less

common forms of thyroid dysfunction in HIV patients, such as subclinical hyperthyroidism and thyroid cancers. In addition, most of the included studies reported that FT3 and FT4 levels had direct correlation with and CD4 counts, while TSH levels inversely correlated with CD4 counts, suggesting that lower CD4 counts are associated with higher TSH levels (Table 1).



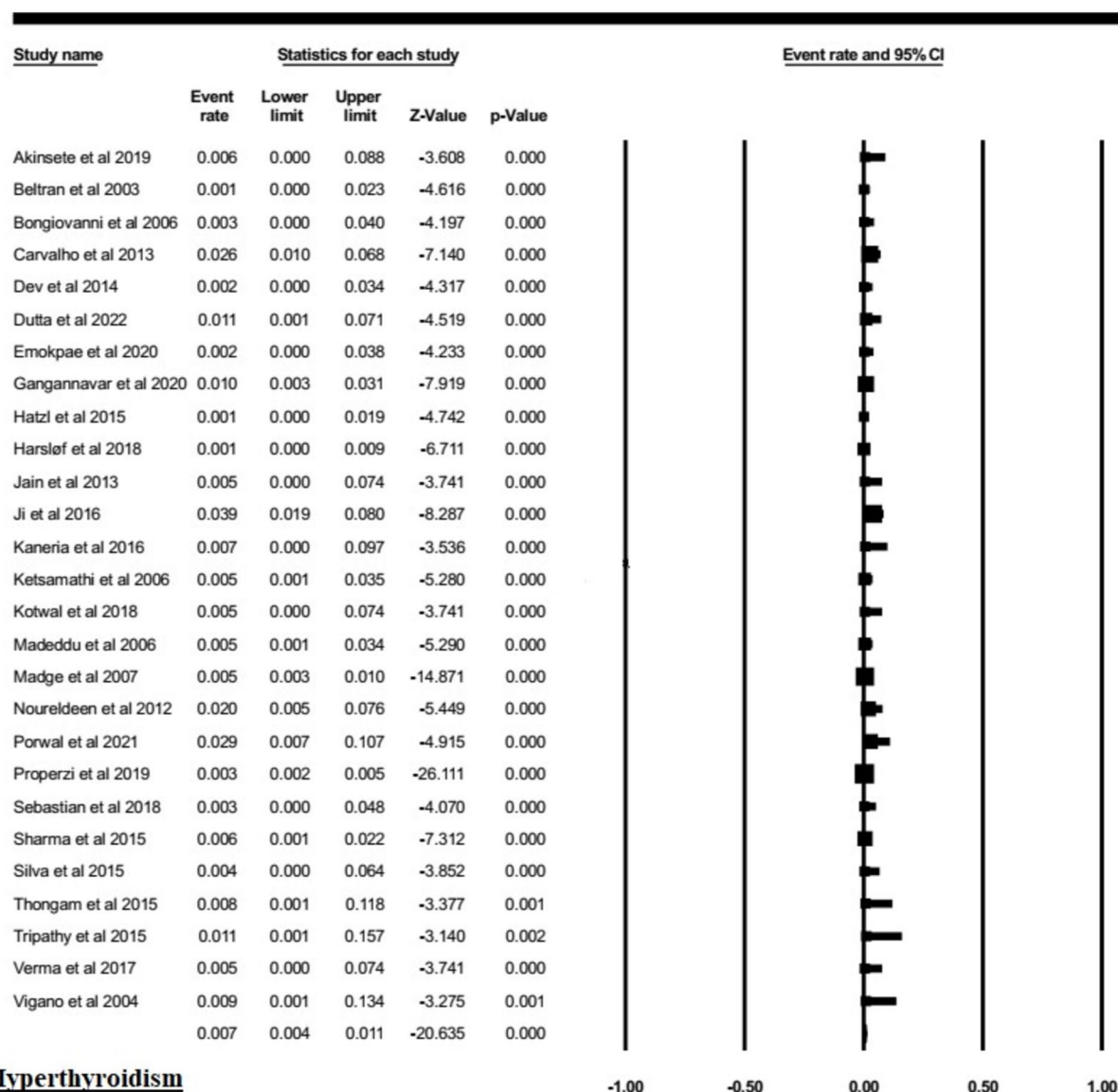
Prevalence of thyroid dysfunction among HIV patients

The meta-analysis for the included studies showed that the overall prevalence of subclinical hypothyroidism among HIV patients was found to be 7.7% (95% confidence interval [CI] 5.0–11.7%) (Fig. 2). The overall prevalence of overt hypothyroidism among HIV patients was 2.7% (95% CI 1.7–4.4%) (Fig. 3). For overt hyperthyroidism, the overall prevalence among HIV patients was found to be 0.7% (95% CI 0.4–1.10%) (Fig. 4). Regarding sick euthyroid syndrome, the overall prevalence of among HIV patients was found to be 2.47% (95% CI 1.2–4.6%) (Fig. 5). The overall prevalence of isolated

hypothyroxinemia (low FT4) among HIV patients was found to be 1.80% (95% CI 0.90–3.30%) (Fig. 6).

Association between thyroid dysfunction and CD4 count

Among the included studies, only four provided sufficient data to calculate the SMD in CD4 count between HIV patients with hypothyroidism and HIV patients without thyroid dysfunction. The pooled effect size analysis demonstrated that HIV patients with hypothyroidism had significantly lower CD4 count compared to HIV patients without thyroid dysfunction, with an SMD of -0.604 (95% CI, -0.947 to -0.257 , $p < 0.001$). (Fig. 7).



Hyperthyroidism

Fig. 4 Pooled prevalence of overt hyperthyroidism in patients with HIV

Thyroid hormones levels

Some of the included studies provided sufficient data to assess the differences in thyroid hormones levels between patients with HIV and healthy controls. In general, the main finding was that only FT4 showed a statistically significant difference between the groups. There were no significant differences between patients with HIV and healthy controls in levels of TSH, T3, T4, and FT3. Among the included studies, nine provided sufficient data to calculate the SMD in TSH levels between patients with HIV and healthy controls and the pooled SMD was -1.294 (95% CI, 0.685 to 0.470, $p=0.059$) (Fig. 7). Regarding T3 and T4, there were seven studies

with sufficient data to calculate the SMD of both T3 and T4 estimates between patients with HIV and their controls. The analysis of T3 levels showed that the pooled SMD = 0.188 (95% CI 0.292 to 0.667; $p=0.443$). Regarding the T4 levels, the analysis showed that the pooled SMD = 0.35 (95% CI -0.657 to 1.357 ; $p=0.496$) (Fig. 8).

There were five studies with sufficient data to calculate the SMD of FT3 and FT4 estimates. The analysis of the FT3 levels showed that the pooled SMD = 0.155 (95% CI, -0.483 to 0.792 ; $p=0.634$). Regarding the FT4 levels, the analysis showed that patients with HIV had lower level of FT4 compared to healthy control, with the pooled SMD of -2.086 (95% CI, -3.740 to -0.432 ; $p=0.013$) (Fig. 9).

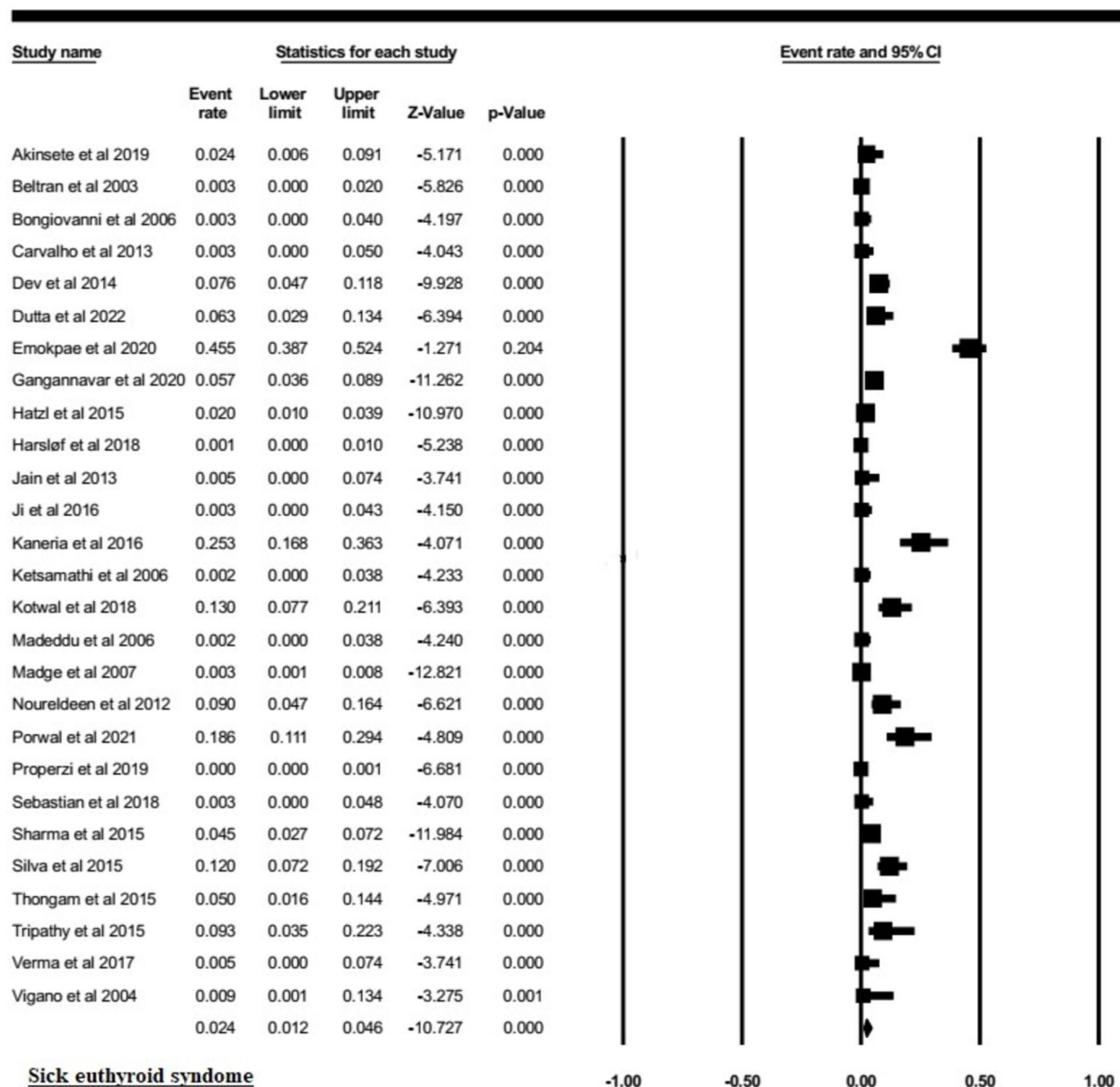


Fig. 5 Pooled prevalence of sick euthyroid syndrome in patients with HIV

Publication bias

Potential publication bias was assessed by examining funnel plots and conducting Begg's and Egger's tests for the analyses (Table 2) (supplementary file 2). The publication bias tests were not significant for most of the thyroid hormone levels. To further investigate and adjust for any potentially missing studies, the Duval and Tweedie trim-and-fill method was applied. This method did not detect any absent and the adjusted prevalence estimates remained consistent with the original findings across all analyses.

Discussion

This review examined the presence of thyroid function abnormalities in patients with HIV infection and its associated factors. The meta-analysis results showed that patients with HIV can develop a variety of thyroid hormone abnormalities, with subclinical hypothyroidism being the most common thyroid abnormality among HIV-positive individuals. The disparity in the reported prevalence rates among the included studies can be attributed to various factors related to the baseline characteristics of the study populations, such as their geographic location, ethnicity, and age distribution.

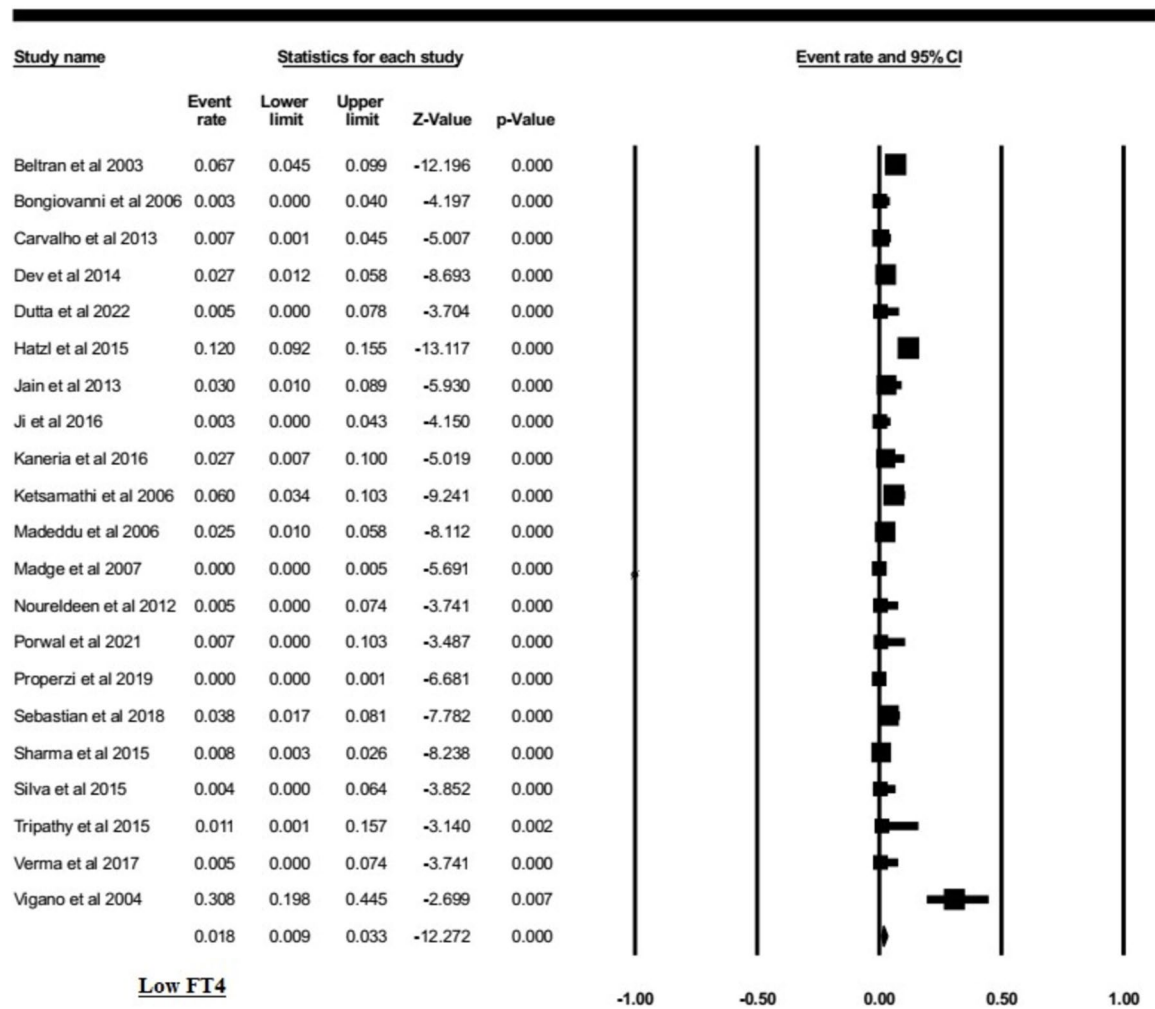


Fig. 6 Pooled prevalence of isolated low FT4 in patients with HIV

The prevalence of clinically manifested thyroid disorders in individuals with HIV appears to be comparable to that reported in a comprehensive review on the global epidemiology of thyroid disease in the general population [11]. Our findings indicate that while thyroid hormone alterations are present in many HIV-positive individuals, the occurrence of clinical or overt thyroid diseases is uncommon. This is further supported by our finding that FT4 was the only thyroid hormone that showed a statistically significant difference between HIV patients and healthy controls. Moreover, most of the thyroid dysfunction identified in our analyses were subclinical or non-thyroidal illness conditions.

Regarding the association between thyroid dysfunction and HIV-related factors, most of the included studies that assessed the relationship between thyroid function abnormalities and low CD4 counts revealed that lower CD4 counts were associated with higher TSH levels, suggesting a link between hypothyroidism

and HIV disease progression. Additionally, individuals with subclinical hypothyroidism had significantly lower CD4 counts compared to those with normal thyroid function. Furthermore, patients with HIV and subnormal levels of FT4 had substantially lower CD4 counts compared to those with normal FT4 levels.

It has been argued that HAART, which is known to be effective in improving the prognosis of HIV, have some effect on the thyroid hormone metabolism. While some of the included studies assessed the impact of HAART on hypothyroidism, the impact of HAART types or duration remains limited and unclear and the reported results from these studies were inconsistent [21, 22, 31, 37, 38]. It is important to note that immune reconstitution syndrome, which occurs when HIV-positive patients after beginning HAART, can sometimes lead to an overactive immune response, which even can trigger or worsen thyroid diseases, causing various autoimmune diseases, including Graves' disease [8, 42, 48]. The restoration

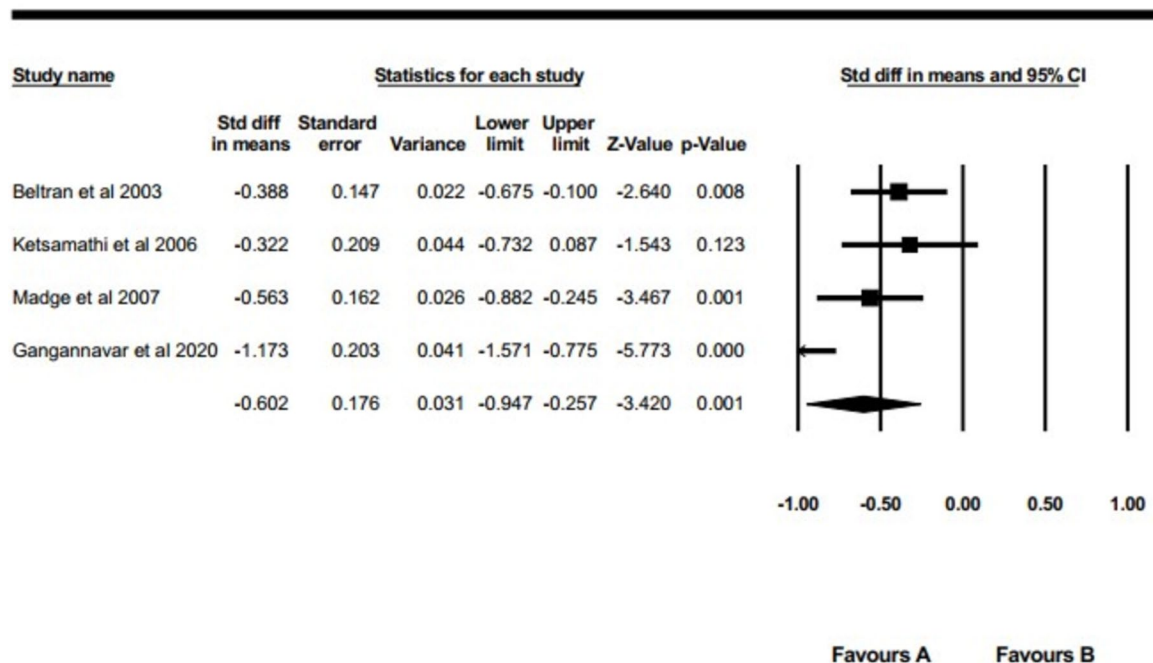


Fig. 7 SMD of CD4 count between HIV patients with hypothyroidism and HIV patients without thyroid dysfunction

of immune function following HAART can cause the immune system to mount an excessive response, which attack the thyroid gland, leading to thyroid dysfunction.

From a clinical perspective, the findings of this review have practical implications. Firstly, the results of this review, showing a low prevalence of overt thyroid dysfunction, reaffirm reports that do not recommend routine thyroid function testing for all HIV patients. Although some studies recommended regular monitoring thyroid function for HIV patients, there is no consensus on routinely assessing thyroid function in all asymptomatic individuals living with HIV [38]. Moreover, the current clinical guidelines typically recommend levothyroxine treatment only in cases where hypothyroidism is overtly manifested or if the TSH exceeded 10 mIU/L [15]. However, thyroid function testing can be considered for individuals with risk factors for thyroid dysfunction and its complications such as pregnant women [51].

Additionally, the review's results indicate that individuals with advanced HIV infection could benefit from thyroid function monitoring due to the noted association between low CD4 count and thyroid dysfunction. Furthermore, the review's findings suggest that for patients with advanced HIV infection and abnormal thyroid function test results, the possibility of non-thyroidal illness caused by advanced HIV infection itself should always be considered. Although overt thyroid problems

are uncommon in HIV patients, subclinical thyroid dysfunction can still significantly impact their health. This is because subclinical hypothyroidism can progress to a more serious form, especially in those with advanced HIV and low CD4 count.

The key limitations of this review are limitations in the available data, as well as, the heterogeneity of the methods used by the included studies to measure and describe data. Variations in study design, such as differences in population characteristics and methodologies, may have introduced potential bias. The exclusion of studies focusing on specific subgroups, such as individuals with HIV/TB or HIV/HCV co-infections, may have excluded valuable insights into these populations. Additionally, there were limited data regarding influence of different HIV stages and specific HAART regimens, such as Stavudine, on thyroid functions in HIV patients. These limitations restrict our ability to conduct additional meta-analyses to explore other aspects of the thyroid functions in HIV patients. Lastly, the inclusion of only English-language publications may limit overall representativeness of the findings of this review. More longitudinal research is needed to have a better understanding of the impact and progression of thyroid disorders in individuals living with HIV, taking into account differences in HIV stages, HAART regimens, and other comorbid conditions.

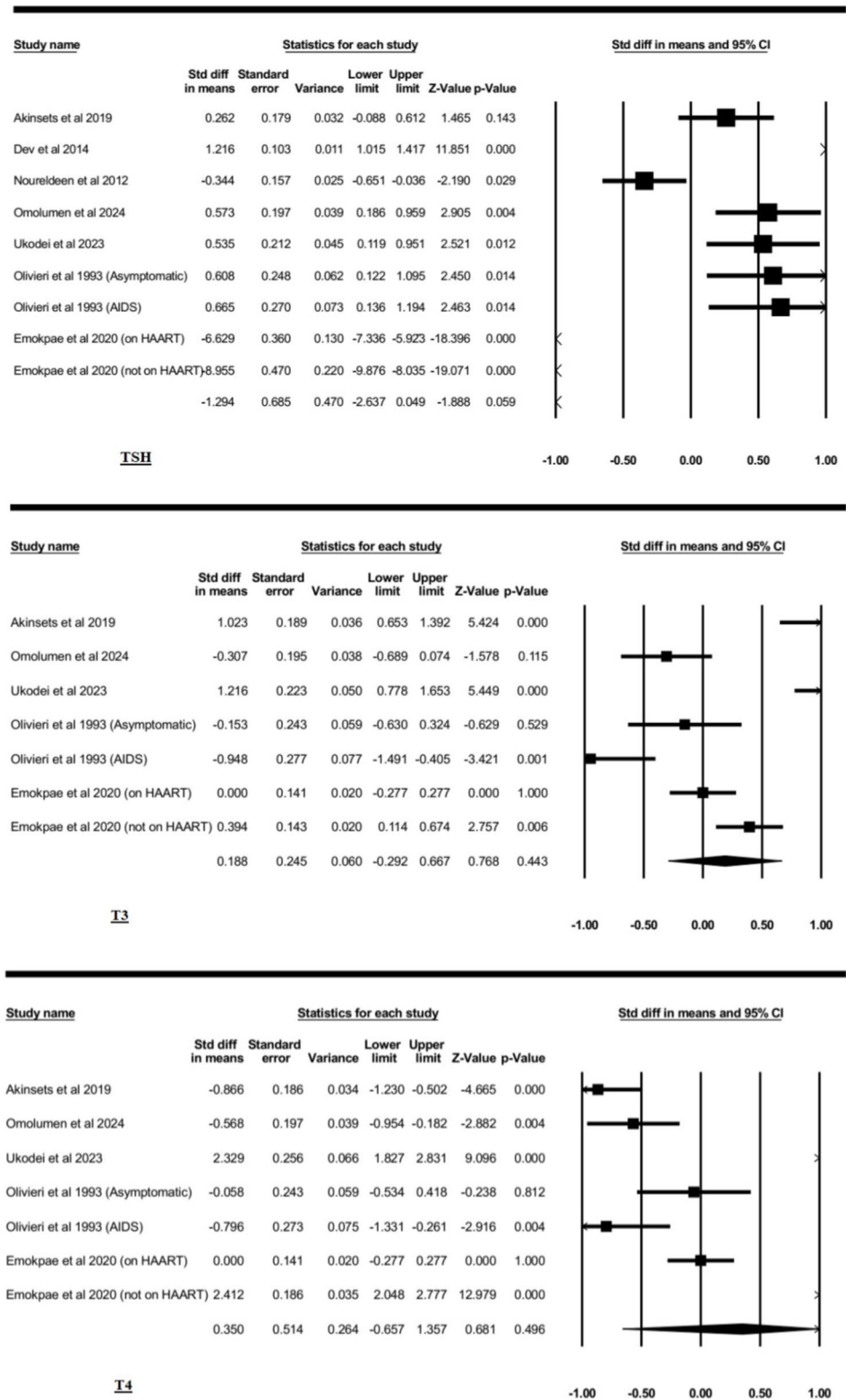


Fig. 8 Pooled SMD of TSH, T3, and T4 estimates between patients with HIV and their controls

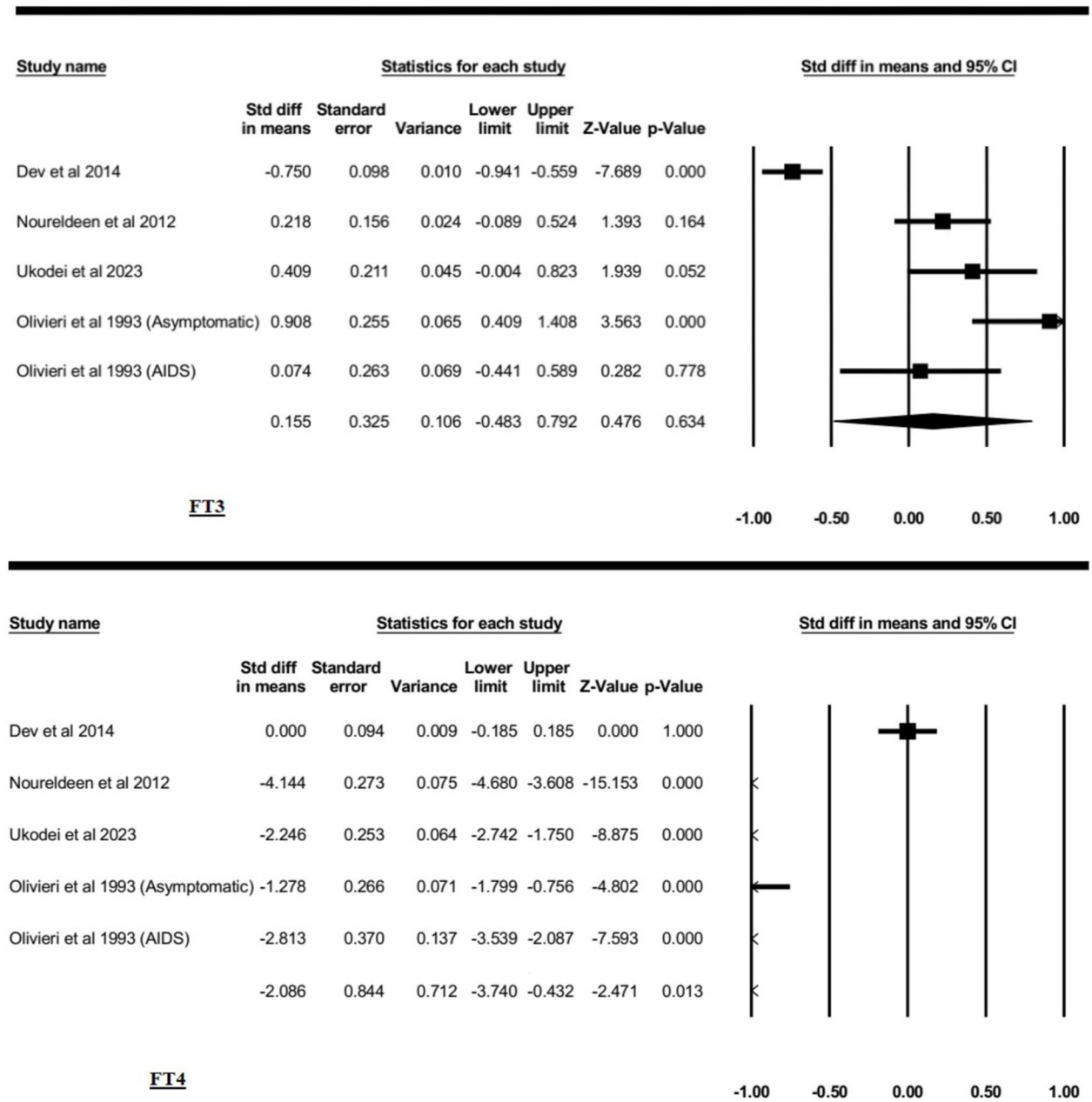


Fig. 9 Pooled SMD of FT3 and FT4 estimates between patients with HIV and their controls

Conclusion

The studies suggest that while thyroid hormones alterations are present in many HIV-positive individuals, the occurrence of clinical thyroid diseases is uncommon. Though, thyroid functions in HIV patients or those with advanced disease or immunosuppression, should be

monitored due to the potential for progression to overt hypothyroidism and associated adverse health outcomes. Additional research is necessary to establish a definitive understanding of the thyroid functions abnormalities in individuals living with HIV, especially in those with severe immune suppression.

Table 2 Results of publication bias and heterogeneity

Outcomes	Begg's test (p value)	Egger's test (p value)	Heterogeneity (I-squared %)
Subclinical hypothyroidism	0.084	0.029	95.18
Hypothyroidism	0.020	0.393	92.09
Hyperthyroidism	0.135	0.488	55.38
Sick euthyroid syndrome	0.174	<0.001	94.06
Low FT4	0.293	<0.001	87.33
TSH level	0.126	0.007	99.07
T3 level	0.382	0.350	91.34
T4 level	0.382	0.413	97.80
FT3 level	0.231	0.023	94.03
FT4 level	0.231	0.022	98.60
CD4 count	0.273	0.367	74.47

Abbreviations

HIV	Human immune deficiency virus
HAART	Highly active anti-retroviral treatments
TSH	Thyroid stimulating hormone;
T3	Triiodothyronine
T4	Thyroxine
FT3	Free T3
FT4	Free T4
SMD	Standardized mean difference

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12981-024-00697-2>.

Supplementary material 1. Search strategy

Supplementary material 2. Funnel plots for detection of publication bias among studies in the meta-analysis of prevalence of subclinical hypothyroidism, overt hypothyroidism, overt hyperthyroidism, sick euthyroid syndrome, and isolated low FT4 in patients with HIV

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Author contributions

SOOM conceptualized the research idea. AAOM, AEAM, YEAE, KFA undertook database searches and articles screening. KSKS, AEBA, KOM, MSKS and MAMA undertook quality assessment. SIEM, DASI, MSKS, and AAOM extracted and summarized data. SOOM analyzed data. SOOM, AABA, SSMS, AIAM, and HAMF interpreted the results and drafted the manuscript. All authors revised, read, and approved the final manuscript.

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Availability of data and materials

No datasets were generated or analysed during the current study.

Declarations**Ethics approval and consent to participate**

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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