Thyrotoxicosis in Africa: a systematic review and meta-analysis of the clinical presentation

Taoreed Adegoke Azeez1*, Tajudin Adesegun Adetunji2 and Mosunmoluwa Adio3

Abstract

Background: Thyrotoxicosis is a common endocrine disorder. The clinical presentation is variable, and it is often misdiagnosed or diagnosed late in Africa. This study was aimed at collating and analyzing the clinical characteristics of the disease across the continent so as to enhance correct and timely diagnosis.

Methods: The study is a systematic review with a meta-analysis. Studies, done in Africa, which documented the clinical features of thyrotoxicosis were selected. African Journal Online (AJOL), PubMed, SCOPUS and Google Scholar, Research Square, SciELO, and medRxiv were systematically searched using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The study quality was assessed using the Newcastle-Ottawa scale. Heterogeneity was determined using $I^2$ statistic and Cochran’s $Q$ test. LFK index and the symmetry of the Doi plot were used to assess publication bias.

Results: The eligible studies were 59 and the total sample size was 9592. The most common symptoms of thyrotoxicosis on the continent included palpitations (69%), weight loss (65%), heat intolerance (64%), tiredness (49%), increased appetite (49%), hyperhidrosis (48%), and insomnia (47%). The most common signs were thyromegaly (88%), tachycardia (67%), sweaty palms (54%), hand tremor (49%), and exophthalmos (49%). Atrial fibrillation, heart failure, and thyrotoxic heart disease were found in 9, 12, and 22% respectively. Other findings were hypertension (25%) and diabetes (9%).

Conclusion: Clinical presentation of thyrotoxicosis varies, and understanding these peculiarities would mitigate misdiagnosis and delayed diagnosis in Africa.

Keywords: Thyrotoxicosis, Clinical presentation, Africa, Meta-analysis, Signs and symptoms, Systematic review

Introduction

The thyroid gland is a bilobed endocrine gland located in the anterior neck. It produces levothyroxine (T4) and liothyronine (T3) which have myriads of cellular effects across the various organ systems [1]. Thyroid hormones are essential for optimal metabolism in human cells [2]. The effects of thyroid hormones on various organ systems are depicted in Table 1. Understanding the physiological effects of thyroid hormones helps to rationalize the possible signs and symptoms of thyroid dysfunction. Excessive or insufficient circulatory levels of thyroid hormones are associated with a variety of symptoms and signs [3]. These signs and symptoms help to identify specific thyroid disorders [4]. Thyroid disorders are the second most common category of diseases seen by Endocrinologists [5, 6]. Thyrotoxicosis is one of the most common thyroid disorders encountered in clinical practice [7].

Thyrotoxicosis is a clinical syndrome characterized by a hypermetabolic state as a result of excess levels of thyroid hormones in the circulation [8, 9]. Based on the statistics from different countries around the globe, as shown in Table 2, the global prevalence of thyrotoxicosis is 0.1–3.4% [10–25, 28, 29]. Common causes of thyrotoxicosis
include Graves’ disease, toxic multinodular goiter and toxic adenoma [28]. Other uncommon causes include thyroiditis, thyroid cancer, thyrotropinoma, medications (like Amiodarone) and struma ovarii [29].

In a bid to make a diagnosis of thyrotoxicosis, there is a need to identify the clinical characteristics of the patients. In Africa, it is still believed that autoimmune diseases, generally, are not as common as what is seen in the western world and the hygiene hypothesis has been postulated as a possible explanation [30]. Graves’ disease, an autoimmune disorder and the most common cause of thyrotoxicosis, is said to be less common in the developing world and this is partly due to the hygiene hypothesis [31]. There is also a strong possibility of underdiagnosis, misdiagnosis and cultural beliefs leading to apparently low incidence among Africans.

Interestingly, as a result of low iodine intake, the proportion of toxic multinodular goiter and toxic adenoma as a cause of thyrotoxicosis is relatively higher in developing nations when compared to the developed world [32]. Similarly, it has been reported that the clinical presentation as well as cardiovascular prognosis of toxic multinodular goiter is different from that of Graves’ disease [33]. Since the proportion of toxic multinodular goiter is higher among African patients with thyrotoxicosis and patients with toxic multinodular goiter present differently, it would be of scientific interest to analyze how Africans with thyrotoxicosis present clinically. This would enhance the accuracy of diagnosis and prognosis in such

### Table 1: Physiological effects of thyroid hormones

| Organ system      | Effects of thyroid hormones                                                                 |
|-------------------|---------------------------------------------------------------------------------------------|
| Cardiovascular    | Inotropic                                                                                   |
|                   | Chronotropic                                                                               |
|                   | Increase cardiac output                                                                     |
|                   | Increase blood pressure                                                                     |
| Respiratory       | Stimulate respiratory drive                                                                  |
|                   | Increase minute ventilation                                                                 |
|                   | Enhances hypoxic and hypercapnic drive of respiration                                        |
|                   | Increase tissue oxygenation                                                                  |
| Gastrointestinal  | Enhances peristalsis                                                                        |
|                   | Promote glucose absorption                                                                  |
| Hepatobiliary     | Increase hepatic low-density lipoprotein (LDL) receptor expression                          |
|                   | Increase cholesterol metabolism and biliary excretion                                        |
|                   | Enhance gall bladder contractility                                                          |
|                   | Increase the synthesis of liver enzymes                                                     |
| Renal             | Needed for kidneys growth and development                                                   |
|                   | Increase glomerular filtration rate                                                         |
|                   | Promote urine concentration and dilution                                                     |
|                   | Affect renal handling of electrolytes                                                       |
| Reproductive      | Male:                                                                                       |
|                   | Enhances the development of the testicles                                                   |
|                   | Promote spermatogenesis                                                                     |
|                   | Affect erectile function                                                                    |
|                   | Affect seminal volume                                                                      |
|                   | Female:                                                                                     |
|                   | Modulate the development of the ovaries, Fallopian tubes and the uterus                    |
|                   | Regulate menstrual cycle                                                                    |
|                   | Promote intrauterine growth of fetuses                                                      |
|                   | Modulate fertility                                                                          |
| Nervous           | Essential for brain development and nerve maturation                                         |
|                   | Important for motor co-ordination                                                          |
|                   | Modulate psychoaffective functioning                                                        |
|                   | Regulate the autonomic nervous system                                                       |
| Musculoskeletal   | Influence bone growth and development                                                      |
|                   | Regulate bone strength                                                                      |
|                   | Affect osteotendinous reflexes                                                              |
|                   | Modulate muscular contraction                                                               |
|                   | Regulate skeletal muscle energy turnover                                                     |
| Integumentary      | Regulate keratinocytes proliferation                                                        |
|                   | Control homeostasis                                                                         |
| Immune system     | Regulate the cellular immune response                                                       |
|                   | Contribute to inflammatory response                                                         |

### Table 2: Prevalence of thyrotoxicosis

| Country                      | Prevalence (%) |
|------------------------------|----------------|
| Australia [10]               | 0.3            |
| Brazil [11]                  | 0.7            |
| Cameroon [12]                | 0.5            |
| China [13]                   | 0.78           |
| Croatia [14]                 | 0.1            |
| Guinea [15]                  | 3              |
| India [5]                    | 1.3            |
| Iran [16]                    | 0.69           |
| Italy [17]                   | 0.76           |
| Libya [18]                   | 0.84           |
| New Zealand [19]             | 0.2            |
| Nigeria [20]                 | 1.4            |
| Paraguay [21]                | 2              |
| Saudi Arabia [22]            | 1.2            |
| South Korea [23]             | 2              |
| Sudan [24]                   | 3.4            |
| Republic of Benin [25]       | 0.87           |
| United Kingdom [26]          | 1.1            |
| USA [27]                     | 0.5            |
patients. To the best of the authors’ knowledge, there has been no multinational study or systematic review to critically examine how the generality of thyrotoxic individuals present clinically in Africa, hence the need for the present study. This study aims to do a systematic review and meta-analysis of the clinical features of patients with thyrotoxicosis across the continent of Africa.

Methods
The study is a systematic review with a meta-analysis. Studies that documented the clinical features of thyrotoxicosis up till March 2022 were selected. Other selection criteria stipulated that the studies (or at least the abstract) must have been reported in English language and must have been carried out in an African country.

The sources of the data used include biomedical databases such as African Journal Online (AJOL), PubMed, SCOPUS, and Google Scholar. Other databases such as Research Square, SciELO, and medRxiv were also searched. A concerted effort was also made to search the gray literature. In searching for the relevant articles, the Preferred Reporting Items for Systematic Reviews and Meta- Analyses (PRISMA) guidelines were strictly followed. The search terms used were “each African country”, “clinical”, “features”, “presentation”, “signs”, “symptoms”, and “thyrotoxicosis”. Others were “hyperthyroidism”, “toxic”, “goitre”, “Graves’ disease”, “Basedow’s disease”, “Plummer’s disease”, “thyroiditis”, “adenoma”, and “thyroid”. In order to enhance the output of the database search, the Boolean operators “AND,” “OR,” and “NOT” were utilized.

![Fig. 1 The PRISMA flow diagram](image-url)
| Study | Sample size | Country | Year | Study type |
|-------|-------------|---------|------|------------|
| 1     | Olurin [36] | 46      | Nigeria | 1972  | Retrospective |
| 2     | Abdulkadir et al [37] | 46 | Ethiopia | 1982 | Prospective |
| 3     | Mengistu [38] | 163 | Ethiopia | 1993 | Prospective |
| 4     | Niakara et al [39] | 32 | Burkina Faso | 2000 | Retrospective |
| 5     | Akosou et al [40] | 82 | Togo | 2001 | Retrospective |
| 6     | Sigilai [41] | 162 | Kenya | 2003 | Retrospective |
| 7     | Mohammed [42] | 49 | Sudan | 2004 | Prospective |
| 8     | Osime & Okobia [43] | 50 | Nigeria | 2004 | Retrospective |
| 9     | Chuhwak & Obekpa [44] | 103 | Nigeria | 2006 | Retrospective |
| 10    | Ogbena et al [45] | 103 | Nigeria | 2007 | Prospective |
| 11    | Ogbena et al [46] | 78 | Nigeria | 2007 | Retrospective |
| 12    | Okosiem et al [47] | 69 | Nigeria | 2007 | Prospective |
| 13    | Sidibe et al [48] | 38 | Mali | 2007 | Cross-sectional |
| 14    | Ali & Na'a'aya [49] | 174 | Nigeria | 2009 | Retrospective |
| 15    | Hattaoui et al [50] | 36 | Morocco | 2009 | Prospective |
| 16    | Ali et al [51] | 53 | Nigeria | 2012 | Prospective |
| 17    | Kebede et al [52] | 233 | Ethiopia | 2012 | Cross-sectional |
| 18    | Onyenekwe [53] | 172 | Nigeria | 2013 | Retrospective |
| 19    | Jaja & Yarhere [54] | 5 | Nigeria | 2014 | Retrospective |
| 20    | Ajabare [55] | 47 | Nigeria | 2015 | Cross-sectional |
| 21    | Dionadi [56] | 125 | Chad | 2015 | Retrospective |
| 22    | Ekpebegh et al [57] | 57 | South Africa | 2015 | Cross-sectional |
| 23    | Balde et al [58] | 49 | Guinea | 2016 | Retrospective |
| 24    | Diagne et al [59] | 108 | Senegal | 2016 | Retrospective |
| 25    | Edo et al [60] | 35 | Nigeria | 2016 | Retrospective |
| 26    | Ogun & Adeleye [61] | 75 | Nigeria | 2016 | Cross-sectional |
| 27    | Sarr et al [62] | 878 | Senegal | 2016 | Retrospective |
| 28    | Ackuaku-Dogbe et al [63] | 116 | Ghana | 2017 | Cross-sectional |
| 29    | Boiro et al | 239 | Senegal | 2017 | Retrospective |
| 30    | Debebe et al [64] | 51 | Ethiopia | 2017 | Retrospective |
| 31    | Anakwue [65] | 50 | Nigeria | 2018 | Prospective |
| 32    | Ayandipo [66] | 228 | Nigeria | 2018 | Retrospective |
| 33    | Azagoh-Kouadio et al [67] | 27 | Cote d'Ivoire | 2018 | Retrospective |
| 34    | Darouassi et al [68] | 60 | Morocco | 2018 | Retrospective |
| 35    | Diedhiou et al [69] | 624 | Senegal | 2018 | Retrospective |
| 36    | El-Shareif [70] | 145 | Libya | 2018 | Retrospective |
| 37    | Sarfo-Kantanka et al [71] | 182 | Ghana | 2018 | Cross-sectional |
| 38    | Gebreyohannes et al [72] | 211 | Ethiopia | 2019 | Retrospective |
| 39    | Isah [73] | 352 | South Africa | 2019 | Retrospective |
| 40    | Mohammed & Hassanein [74] | 60 | Egypt | 2019 | Experimental |
| 41    | Mulatu [75] | 146 | Ethiopia | 2019 | Cross-sectional |
| 42    | Ojo et al [76] | 38 | Nigeria | 2019 | Cross-sectional |
| 43    | Okafor et al [20] | 151 | Nigeria | 2019 | Prospective |
| 44    | Toyib et al [77] | 33 | Ethiopia | 2019 | Cross-sectional |
| 45    | Yazidi et al [78] | 538 | Tunisia | 2019 | Retrospective |
| 46    | Adeleye et al [79] | 61 | Nigeria | 2020 | Retrospective |
| 47    | Boundia et al [80] | 1040 | Senegal | 2020 | Retrospective |
| 48    | Demba et al [81] | 210 | Senegal | 2020 | Retrospective |
| 49    | Ersumo et al [82] | 589 | Ethiopia | 2020 | Retrospective |
The authors independently scrutinized the retrieved studies, and those that met the inclusion criteria were added to the systematic review. Data were initially collated using a Microsoft Excel spreadsheet (Redmond, Washington, USA), and the meta-analysis analysis was done using Meta XL version 5.3 (EpiGear International Ltd., Northwestern University, Sunrise Beach, Queensland, Australia.) which is add-in software for Microsoft Excel. The DerSimonian Laird random effect model was used for the meta-analysis.

The quality of the selected studies was assessed using the Newcastle-Ottawa scale. Using the Agency for Healthcare Research and Quality (AHRQ) standards, 76% of the studies were good, 19% were adequate, and 5% were poor. The heterogeneity of the selected studies was determined using $I^2$ statistic and Cochran’s $Q$ test. $I^2$ values of 25%, 50%, and 75% correspond to small, moderate, and large amounts of heterogeneity respectively [34]. Q statistic value of 75–100 is considered as substantial heterogeneity [35]. LFK index and the symmetry of the Doi plot were used to assess publication bias. Figure 1 shows the PRISMA flow diagram for the systematic review.

**Results**

Fifty-nine studies met the eligibility criteria and were eventually selected. The characteristics of the studies are shown in Table 3. The studies cut across different regions of Africa. The total sample size was 9592. As shown in Fig. 2, most of the studies were retrospective and cross-sectional in design. The studies were mostly carried out between 1972 and 2022. Table 4 shows the mean age and the female-to-male ratio of the selected studies. The pooled mean age is 37.8 years. The pooled female-to-male ratio among individuals with thyrotoxicosis in Africa is 6.4:1. Table 5i–iii shows the symptoms of thyrotoxicosis among African patients.
The pooled frequencies of the symptoms of thyrotoxicosis among Africans are shown in Table 6. Figures 3, 4, 5, and 6 represent the forest plots of the symptoms while Figs. 7, 8, and 9 represent the corresponding Doi plots. Figure 10 shows the symptoms of thyrotoxicosis among African patients in order of frequency. The commonest symptoms are palpitations, heat intolerance, and weight loss.

Table 7 shows some general signs in Africans with thyrotoxicosis. Table 8 shows the frequencies of some cardiovascular and neurological manifestations of thyrotoxicosis among Africans. Table 9 shows the frequencies of the eye manifestations in thyrotoxicosis. Other eye signs included Joffroy's sign, Goldzieher's sign, and Hertoge's sign. Table 10 shows the cardiometabolic morbidities seen in patients with thyrotoxicosis across Africa. The pooled frequencies of the various signs of thyrotoxicosis are shown in Table 11. Figures 11, 12, 13, 14, and 15 represent the forest plots of the signs while Figs. 16, 17, 18, 19, and 20 represent the corresponding Doi plots. Figure 21 shows the signs of thyrotoxicosis among African patients in order of frequency. Figure 22 shows the pooled frequencies of cardiometabolic morbidities in Africans with thyrotoxicosis.

Discussion

Based on the eligibility criteria, only 59 studies could be analyzed. Interestingly, most of the studies were even in the last two decades. It has been reported that thyrotoxicosis was relatively rare (or underdiagnosed) in Africa which might partly explain this trend in the prevalence of the disease [36]. In addition, Africa is experiencing a transition from iodine deficiency to...

### Table 4: Mean age and the sex ratio of the selected studies

| Studies | Sample size | Mean age (years) | F:M |
|---------|-------------|------------------|-----|
| 1 Olurin [36] | 46 | NA | 3.6:1 |
| 2 Abdulkadir et al [37] | 46 | 30.0 | 4.9:1 |
| 3 Mengistu [38] | 163 | NA | 8:1 |
| 4 Niakara et al [39] | 32 | 42.2 | 3.4:1 |
| 5 Akossou et al [40] | 82 | NA | NA |
| 6 Sigila [41] | 162 | 37.0 | 4:2:1 |
| 7 Mohammed [42] | 49 | NA | 5.7:1 |
| 8 Osime & Okobia [43] | 50 | 32.0 | 15.7:1 |
| 9 Chuhwak & Obekpa [44] | 103 | 38.6 | 9:1 |
| 10 Ogbera et al [45] | 103 | 40.8 | 5:1 |
| 11 Ogbera et al [46] | 78 | 40.0 | 5.6:1 |
| 12 Okosime et al [47] | 69 | 37.8 | 3.9:1 |
| 13 Sidibe et al [48] | 38 | 12.5 | 3:1 |
| 14 Ali & Na'aya [49] | 174 | 33.9 | 7.8:1 |
| 15 Hattaoui et al [50] | 36 | 44.5 | NA |
| 16 Ali et al [51] | 53 | 30.8 | 6:1 |
| 17 Kebede et al [52] | 233 | 43.1 | 9:1 |
| 18 Onyenekwe [53] | 172 | 40.2 | 4:1 |
| 19 Jaja & Yarhere [54] | 5 | NA | 1.5:1 |
| 20 Dionadji [55] | 125 | 35.7 | 5:1 |
| 21 Ekebegghe et al [57] | 57 | 39.7 | 9:1 |
| 22 Balde et al [58] | 49 | 42.0 | 15.3:1 |
| 23 Diagne et al [59] | 108 | 34.6 | 7.3:1 |
| 24 Edo et al [60] | 35 | 44.3 | 10.6:1 |
| 25 Ogun & Adeleye [61] | 75 | 42.0 | 5.3:1 |
| 26 Sarr et al [62] | 878 | 34.8 | 4:2:1 |
| 27 Ackuaku-Dogbe et al [63] | 116 | 45.2 | 4:5:1 |
| 28 Boiro et al [64] | 239 | 10.8 | 2.8:1 |
| 29 Debebe et al [64] | 51 | 30.0 | NA |
| 30 Anakvue [65] | 50 | 44.0 | NA |
| 31 Ayandipo [66] | 228 | 38.0 | 5:8:1 |
| 32 Azagoh-Kouadio et al [67] | 27 | NA | 4.4:1 |
| 33 Daroussi et al [68] | 60 | 52.0 | NA |
| 34 Diedhiou et al [69] | 624 | 32.1 | NA |
| 35 El Shareef [70] | 145 | 36.8 | 2.5:1 |
| 36 Sarfo-Kantanka et al [71] | 182 | 39.9 | 5:1:1 |
| 37 Gebreyohannes et al [72] | 211 | 47.3 | 9.4:1 |
| 38 Isah [73] | 352 | NA | 7:3:1 |
| 39 Mohammed & Hassanein [74] | 60 | 38.2 | 7.6:1 |
| 40 Mulatu [75] | 146 | 47.2 | 13:1 |
| 41 Ojo et al [76] | 38 | NA | NA |
| 42 Okafor et al [20] | 151 | 49.2 | 6.5:1 |
| 43 Toyib et al [77] | 33 | 41.8 | 7.9:1 |
| 44 Yazidi et al [78] | 538 | NA | NA |
| 45 Adeleye et al [79] | 61 | 45.0 | 9:1 |
| 46 Boundia et al [80] | 1040 | 31.5 | 3.3:1 |
| 47 Demba et al [81] | 210 | 65.3 | 5.7:1 |

**Table 4 (continued)**

| Studies | Sample size | Mean age (years) | F:M |
|---------|-------------|------------------|-----|
| 48 Ersumo et al [82] | 589 | 40.0 | 7.9:1 |
| 49 Mariko et al [83] | 70 | 13.1 | 6.25:1 |
| 50 Mohammed [84] | 159 | 43.7 | 6.3:1 |
| 51 Ahera et al [85] | 89 | 45.0 | 9:1 |
| 52 Docrat et al [86] | 171 | 43.2 | 5:3:1 |
| 53 Kifle et al [87] | 211 | NA | 13:1 |
| 54 Maldey et al [88] | 336 | 46.7 | 8:1 |
| 55 Mendes [89] | 31 | 10.1 | 5.2:1 |
| 56 Roto [90] | 124 | 40.5 | 11:1 |
| 57 Syia et al [91] | 26 | 52.8 | 2.7:1 |
| 59 Balde et al [92] | 156 | 39.4 | 13:3 |

F:M female-to-male ratio, NA not available
| Study                                      | Weight loss (%) | Heat intolerance (%) | Excessive sweating (%) | Palpitations (%) | Tiredness (%) | Increased appetite (%) |
|--------------------------------------------|-----------------|---------------------|------------------------|-----------------|--------------|------------------------|
| Olurin [36]                                | 74.0            | –                   | 70.0                   | –               | –            | 41.0                   |
| Abdulkadir et al [37]                      | 84.6            | 82.6                | 82.6                   | 82.6            | –            | –                      |
| Sigilai [41]                               | 60.0            | 56.0                | –                      | 52.0            | 24.0         | 31.0                   |
| Mohammed [42]                              | 23.0            | 70.0                | –                      | 35.0            | 10.0         | 25.0                   |
| Osmie & Okobia [43]                        | 90.0            | 84.0                | –                      | 86.0            | –            | 100                    |
| Chuhwak & Obekpa [44]                      | 50.0            | –                   | –                      | 49.0            | –            | –                      |
| Ogbera et al [46]                          | 63.4            | 68.0                | 57.0                   | 58.7            | 63.4         | 53.0                   |
| Sidibe et al [48]                          | 31.5            | –                   | –                      | 34.4            | –            | –                      |
| Ali & Na'aya [49]                          | 39.7            | 28.8                | –                      | 35.8            | –            | 14.1                   |
| Ali et al [51]                             | 79.0            | 78.7                | –                      | 94.0            | –            | 78.0                   |
| Kebede et al [52]                          | –               | 81.9                | –                      | 96.0            | –            | –                      |
| Onyenekwe [53]                             | 86.0            | 82.0                | 67.4                   | 81.4            | 54.7         | 61.2                   |
| Jaja & Ivahre [54]                         | 100             | –                   | –                      | 20.0            | –            | 14.1                   |
| Ajibare [55]                               | 85.0            | 85.0                | 100                    | 95.5            | –            | –                      |
| Dionadiji [56]                             | 80.8            | –                   | 31.2                   | –               | –            | –                      |
| Balde et al [58]                           | 73.0            | –                   | –                      | –               | –            | –                      |
| Diagne et al [59]                          | 39.8            | –                   | –                      | 46.3            | –            | –                      |
| Edo et al [60]                             | 60.0            | 37.1                | –                      | 60.0            | –            | –                      |
| Ogun & Adeleye [61]                        | 63.8            | –                   | 52.0                   | 59.4            | 32.0         | 35.0                   |
| Sarr et al [62]                            | 79.9            | 53.3                | –                      | 83.1            | 53.6         | 50.1                   |
| Biore et al [63]                           | 69.8            | –                   | –                      | –               | –            | –                      |
| Debebe et al [64]                          | 4.0             | 31.4                | 9.8                    | 47.1            | –            | –                      |
| Anakwue [65]                               | 48.0            | 46.0                | 38.0                   | 60.0            | –            | 32.0                   |
| Ayandipo [66]                              | 74.0            | 84.0                | –                      | –               | –            | –                      |
| Azagoh-Kouadio et al [67]                  | 81.5            | 30.0                | 26.0                   | 81.5            | –            | –                      |
| Darouassi et al [68]                       | 39.5            | 15.1                | 20.6                   | –               | 68.3         | –                      |
| Diedhiou et al [69]                        | 51.4            | –                   | –                      | –               | –            | –                      |
| El-Shafei [70]                             | 54.5            | 35.2                | 36.6                   | 53.1            | 18.6         | –                      |
| Sarfo-Kantanka et al [71]                  | 80.0            | 76.0                | 76.0                   | 80.0            | 80.0         | –                      |
| Gebreyohannes et al [72]                   | 27.0            | 70.1                | 52.2                   | 83.4            | 37.9         | 14.7                   |
| Ojo et al [76]                             | 100             | 73.7                | 100                    | 86.8            | –            | –                      |
| Okofor et al [20]                          | 80.0            | 86.0                | 72.0                   | 74.0            | 80.0         | 68.0                   |
| Toyib et al [77]                           | 100             | 100                 | –                      | 100             | –            | –                      |
| Adeleye et al [79]                         | 100             | 100                 | –                      | 100             | –            | –                      |
| Dimba et al [81]                           | 61.9            | –                   | –                      | 66.7            | 37.1         | –                      |
| Ersumo et al [82]                          | 24.8            | –                   | 2.0                    | 7.5             | 36.5         | 8.0                    |
| Mariko et al [83]                          | 87.1            | –                   | –                      | 81.4            | –            | –                      |
| Mohammed [84]                              | –               | 25.8                | 10.7                   | 54.7            | –            | –                      |
| Aberapa et al [85]                         | 35.0            | 59.0                | 44.5                   | 84.5            | 69.0         | 33.0                   |
| Docrat et al [86]                          | 58.0            | 92.0                | 45.0                   | 88.0            | 80.0         | –                      |
| Kifle et al [87]                           | –               | –                   | –                      | 83.9            | –            | –                      |
| Maldev et al [88]                          | –               | 66.3                | –                      | 62.7            | –            | 32.4                   |
| Mendes [89]                                | 54.5            | –                   | –                      | 18.2            | –            | –                      |
| Ruto [90]                                  | 75.8            | –                   | –                      | 75.8            | –            | –                      |
| Sylla et al [91]                           | 68.3            | 15.1                | 20.7                   | –               | –            | –                      |
| Balde et al [92]                           | 89.0            | 81.0                | –                      | 98              | –            | –                      |
### Table 5 (continued)

| Study                      | Hyperdefecation (%) | Insomnia (%) | Nervousness (%) | Irritability (%) | Oligomenorrhea (%) |
|----------------------------|---------------------|--------------|-----------------|------------------|--------------------|
| Olurin [36]                | 47.0                | 19.0         | 63.0            | 63.0             | 7.0                |
| Abdulkadir et al [37]      | –                   | 69.9         | 73.9            | –                | 25.0               |
| Sigilai [41]               | 22.0                | –            | –               | 30.0             | –                  |
| Mohammed [42]              | 13.0                | –            | –               | 35.0             | 15.0               |
| Osime & Okobia [43]        | 24.0                | 97.4         | –               | –                | –                  |
| Chuhwak & Obekpa [44]      | –                   | –            | 44.0            | –                | –                  |
| Ogbe et al [46]            | –                   | –            | 41.0            | –                | 22.0               |
| Ali & Na’a’aya [49]        | –                   | 14.1         | –               | –                | –                  |
| Ali et al [51]             | –                   | –            | –               | –                | 41.0               |
| Onyenekwe [53]             | 74.4                | 47.7         | 51.7            | –                | 24.0               |
| Jaja & Yarhere [54]        | 60.0                | 60.0         | –               | –                | –                  |
| Ajibare [55]               | 61.7                | –            | –               | –                | –                  |
| Ogun & Adeleye [61]        | 32.7                | 46.9         | 57.1            | 42.9             | –                  |
| Sarr et al [62]            | 23.8                | 56.7         | 4.4             | 4.4              | –                  |
| Debebe et al [64]          | –                   | 15.7         | –               | 27.4             | –                  |
| Ayandipo [66]              | –                   | 54.0         | –               | –                | 41.0               |
| Azagoh-Kouadio et al [67]  | 26.0                | 44.0         | 44.0            | –                | 52.0               |
| Darouass i et al [68]      | –                   | –            | –               | 38.9             | –                  |
| El-Shareif [70]            | 9.7                 | –            | –               | 21.4             | –                  |
| Sarfo-Kantanka et al [71]  | 40.0                | 70.0         | 62.0            | –                | 38.0               |
| Gebreychannes et al [72]   | 0.95                | –            | 0.95            | 13.7             | 3.5                |
| Ojo et al [76]             | 78.9                | –            | –               | –                | –                  |
| Okafor et al [20]          | –                   | –            | 52.0            | –                | 25.0               |
| Toyib et al [77]           | 45.0                | 75.8         | –               | –                | –                  |
| Adeleye et al [79]         | 100.0               | –            | –               | –                | –                  |
| Demba et al [81]           | –                   | 47.6         | –               | –                | –                  |
| Ensumo et al [82]          | –                   | –            | –               | 7.1              | –                  |
| Mohammed [84]              | 2.5                 | 3.1          | –               | 11.3             | –                  |
| Ahera et al [85]           | –                   | –            | 55.0            | –                | –                  |
| Maldey et al [88]          | –                   | 61.0         | 27.0            | –                | –                  |
| Mendes [89]                | –                   | –            | –               | 25.5             | –                  |
| Sylla et al [91]           | –                   | –            | –               | 38.9             | –                  |
| Balde et al [92]           | 58.0                | 68.0         | 91.0            | –                | –                  |
| Study                      | Dyspnea             | Psychotic symptoms | Skin darkening | Weight gain | Infertility | Hair loss |
| Olurin [36]                | 19.0                | –            | –               | –                | –                  |
| Sigilai [41]               | 25.0                | 18.0         | –               | –                | –                  |
| Mohammed [42]              | –                   | –            | –               | –                | 10.0               |
| Ogbe et al [45]            | –                   | 1.9          | –               | –                | –                  |
| Ogbe et al [46]            | –                   | –            | 41.0            | –                | –                  |
| Onyenekwe [53]             | –                   | 1.2          | 11.6            | 1.2              | 5.8                |
| Ogun & Adeleye [61]        | –                   | –            | –               | 5.0              | –                  |
| Sarr et al [62]            | –                   | –            | 9.1             | –                | 7.5                |
| Boiro et al                | –                   | –            | 22.1            | –                | –                  |
| Azagoh-Kouadio et al [67]  | 63.0                | –            | –               | –                | –                  |
| Diedhiou et al [69]        | –                   | –            | –               | 3.5              | –                  |
| El-Shareef [70]            | –                   | –            | 2.1             | 2.1              | 14                 |
| Sarfo-Kantanka et al [71]  | 78.0                | –            | 8.0             | –                | –                  |
iodine sufficiency through the universal iodine fortification campaign and this has been associated with increased incidence of autoimmune thyroid disorders [93]. Also, delayed presentation, misdiagnosis, and paucity of experts could translate to falsely low prevalence and lack of interest in studying the disease [94]. Nonetheless, language disparity (as studies selected must have at least the abstract in English to meet the selection criteria) could have also contributed to the relatively limited number of eligible studies.

The study cuts across Africa and a little less than 10,000 people were involved. Considering that autoimmune thyroid disorders, which account for the commonest cause of thyrotoxicosis, are less common among Africans when compared with Caucasians, it can be deduced that the sample size is representative enough and the findings can be applied across the continent [95]. It is not surprising that most of the studies (83%) are retrospective and cross-sectional as these are commonly used to document the frequencies of observations such as signs and symptoms [96]. They are also cheaper and require less logistical outlay which make them suitable for low-resource settings such as Africa [96]. However, it is well known that retrospective studies have recall bias and cross-sectional studies may not be fully representative or establish a cause-effect relationship.

The average age of Africans with thyrotoxicosis was 37.8 years. Other authors have documented an averagely young age among cohorts of people with thyrotoxicosis in different countries [97–99]. Graves’ disease is the most common cause of thyrotoxicosis and it tends to peak between 20 and 50 years [100]. This may partly account for the average age of patients with thyrotoxicosis seen in this study. This study demonstrated that thyrotoxicosis is

| Table 5 (continued) |
|---------------------|
| Gebreyohannes et al [72] | 10.4 | – | – | – | – | – |
| Okafor et al [20] | – | – | 35.0 | – | 74.0 | 27.0 |
| Ersumo et al [82] | 1.0 | 3.7 | – | – | – | – |
| Abera et al [85] | 5.0 | – | – | – | – | – |
| Kifle et al [87] | 86.3 | – | – | – | – | – |
| Balde et al [92] | 98 | – | – | – | – | – |
| –, not available |

| Table 6 Pooled frequency of the symptoms |
|-----------------------------------------|
| Symptoms       | Frequency (%) | 95% CI   | p     | I² (%) | Q statistic | LFK Index |
|---------------|---------------|----------|-------|--------|-------------|-----------|
| Weight loss   | 65            | 60–70    | <0.0001 | 99     | 6097        | −8.29     |
| Heat intolerance | 64          | 58–70    | <0.0001 | 99     | 3250        | −8.90     |
| Palpitations  | 69            | 62–77    | <0.0001 | 100    | 8536        | −5.75     |
| Excessive sweating | 48          | 29–67    | <0.0001 | 100    | 26,649      | −5.3      |
| Tiredness     | 49            | 38–60    | <0.0001 | 98     | 648         | 1.12      |
| Increased appetite | 49          | 38–60    | <0.0001 | 97     | 678         | 1.12      |
| Hyperdefecation | 37           | 23–51    | <0.0001 | 98     | 856         | 1.93      |
| Insomnia      | 47            | 36–59    | <0.0001 | 97     | 595         | −0.8      |
| Nervousness   | 41            | 32–49    | <0.0001 | 99     | 2919        | 8.86      |
| Irritability  | 25            | 16–36    | <0.0001 | 96     | 268         | 5.65      |
| Oligomenorrhea | 23            | 13–34    | <0.0001 | 94     | 181         | 0.15      |
| Dyspnea       | 40            | 7–78     | <0.0001 | 99     | 1582        | 2.58      |
| Psychotic symptoms | 3        | 0–7      | <0.0001 | 92     | 35          | 2.64      |
| Skin darkening | 15            | 6–26     | <0.0001 | 96     | 117         | 2.22      |
| Weight gain   | 3             | 1–5      | <0.0001 | 45     | 3.62        | 0.08      |
| Infertility   | 26            | 0–86     | <0.0001 | 99     | 212         | 1.115     |
| Hair loss     | 13            | 5–24     | <0.0001 | 95     | 82          | 2.92      |
| Pruritus      | 9             | 6–13     | <0.0001 | 1      | 0.3         | –         |
| Persistent headache | 5        | 2–8      | <0.0001 | 30     | 1.43        | –         |
| Menorrhagia   | 5             | 3–8      | <0.0001 | 0      | 0.34        | 1.22      |
about 6 times more common among females compared to males. Data from Asia, Europe, Oceania, and America have corroborated this finding of a significant female preponderance of thyrotoxicosis cases [101–103]. Some of the reasons proposed for this female predominance in thyrotoxicosis include the higher prevalence of autoimmune disorders among females, the role of the female sex hormones, and the rebound immune status in postpartum state (as pregnancy is immunosuppressive) [104].

Fig. 3 Forest plots showing the frequencies of weight loss
The symptoms of thyrotoxicosis seen in Africa vary in frequencies from what is seen in other parts of the world [105, 106]. These differences in frequencies and patterns of presenting features imply that clinicians practicing in Africa need to understand how patients present here. The most common symptoms of thyrotoxicosis in Africa are palpitations, weight loss, heat intolerance, and tiredness. Similar (but not identical) findings have been reported by non-African authors in various studies conducted outside Africa [107, 108]. Other symptoms, found in this study, were increased appetite, excessive sweating, insomnia, nervousness, and pruritus. Again, these are similar to what is found among thyrotoxicosis patients managed in other continents too [109].

Oligomenorrhea is the most common menstrual abnormality but a minority (3%) also have menorrhagia.
Krassas, in Greece, demonstrated, in his study, that oligomenorrhea is quite common in premenopausal women with thyrotoxicosis while Tara, in Iraq, also reported that menorrhagia can rarely occur in thyrotoxicosis [110, 111]. About 1 out of 4 individuals with thyrotoxicosis in Africa present with infertility. Quintino-Moro did a study in Brazil while Krassas did a similar study in Greece and both found a high prevalence...
infertility among female and male hyperthyroid individuals respectively [112, 113].

Again, despite that weight loss is one of the most common symptoms, a minority of thyrotoxicosis patients (3%) present with weight gain. In the thyrotoxic patients experiencing weight gain, it is often due to increased appetite and excess calorie consumption [114]. This usually occurs following the commencement of treatment. The pooled prevalence of psychotic symptoms in the present study is 3%. Some authors, working outside Africa, have also found a similar proportion of thyrotoxic patients presenting with psychotic symptoms [115, 116]. Usually, the psychotic manifestations tend to remit with the treatment of thyrotoxicosis but some may require addition of anti-psychotic drugs.

Based on the findings of this study, enlarged thyroid gland, tachycardia, sweaty palms, and hand tremors are the most common clinical signs seen in a person with thyrotoxicosis in Africa. These manifestations have been documented in other studies and are due to the heightened activities of the sympathoadrenal system in such individuals [117]. In this study, atrial fibrillation was found in 9% of individuals with thyrotoxicosis in Africa. Other studies, outside Africa, have quoted a prevalence rate of 5–15% for atrial fibrillation in thyrotoxicosis and this is similar to the outcome of the present study [118, 119]. Thyrotoxicosis causes a reduction in the repolarization phase of the atria and this predisposes the atrium to fibrillation [120].

Bilateral exophthalmos was found in 49% of Africans with thyrotoxicosis, according to the outcomes of the present study. Retrospective studies done in the UK estimated a proportion of 35–57% of ocular involvement in thyrotoxicosis [121]. Activation of TSH receptors in the ocular tissues by TSH receptor antibodies (TRAb) is
Fig. 8  Doi plot for heat intolerance

Fig. 9  Doi plot for palpitations
believed to be the underlying link between Graves’ disease and thyroid eye changes including exophthalmos [121]. Lid retraction was found in 19% of thyrotoxic Africans. However, in a previous study done in India, a proportion of 28–34% was documented. This may be due to racial differences and the differences in the study protocols [122].

Seven percent of thyrotoxic individuals in this study had pretibial myxedema. It can be found in 5–15% of individuals with Graves’ disease, as reported in some non-African studies [123]. It has variable presentation and can occur before, during, and after the clinical presentation of classical thyrotoxicosis signs and symptoms. Hypertension and diabetes mellitus were found in 25% and 9% respectively of Africans with thyrotoxicosis. Prisant et al., in the USA, reported a prevalence of 10–50% for hypertension in hyperthyroid patients [124]. Due to adrenergic hyperactivity in thyrotoxicosis, there is increased cardiac output from enhanced chronotropic and inotropic effects and this ultimately leads to the rise in blood pressure in thyrotoxicosis [125]. Increased metabolic demand and endothelin-1 secretion in thyrotoxicosis are also possible explanations for hypertension in thyrotoxicosis. Proposed mechanisms for a relatively high prevalence of diabetes mellitus in thyrotoxicosis include concurrence of autoimmune disorders (for type 1 diabetes), enhanced degradation of insulin, increased prandial glucose absorption, increased gluconeogenesis, and insulin resistance [126].

In this study, heart failure was documented in 12% of the individuals with thyrotoxicosis. Previous studies outside Africa have quoted a prevalence of 6–19% for heart failure in thyrotoxicosis [127, 128]. Thyrotoxicosis is associated with certain hemodynamic changes such as increased blood volume which increases preload, and hypertension which increases afterload. There is also an increased incidence of tachyarrhythmia. These are some of the possible reasons thyrotoxicosis is associated with more cases of heart failure compared with the general population.

| Symptoms                  | Frequency (%) |
|---------------------------|---------------|
| Palpitations              | 69            |
| Weight loss               | 65            |
| Heat intolerance          | 64            |
| Tiredness                 | 49            |
| Increased appetite         | 49            |
| Excessive sweating        | 48            |
| Insomnia                  | 47            |
| Nervousness               | 41            |
| Dyspnoea                  | 40            |
| Hyperdefaecation          | 37            |
| Infertility               | 26            |
| Irritability              | 25            |
| Oligomenorrhoea           | 23            |
| Skin...                   | 15            |
| Hair loss                 | 13            |
| Pruritus                  | 9             |
| Menorrhagia               | 5             |
| Persistent headache       | 5             |
| Psychotic symptoms        | 3             |
| weight gain               | 3             |

**Fig. 10** Frequency of thyrotoxicosis symptoms in Africa
### Table 7  General signs of thyrotoxicosis

| Study                          | Goiter (%) | Thyroid bruit (%) | Sweaty palms (%) | Onycholysis (%) | Pretibial myxedema (%) |
|-------------------------------|------------|-------------------|------------------|----------------|------------------------|
| Olurin [36]                   | 93.0       | 33.0              | 78.0             | –              | –                      |
| Abdulkadir et al [37]         | 97.8       | –                 | –                | –              | 18.2                  |
| Sigilai [41]                  | 85.0       | –                 | 28.0             | –              | –                      |
| Mohammed [42]                 | 53.4       | 29.0              | –                | 73.0           | –                      |
| Osme & Okobia [43]            | 100        | –                 | –                | –              | –                      |
| Chuhwak & Obekpa [44]         | 95.0       | –                 | 58.0             | –              | –                      |
| Ogbera et al [45]             | 90.0       | –                 | –                | –              | –                      |
| Ogbera et al [46]             | 97.0       | –                 | 44.0             | –              | –                      |
| Sidibe et al [48]             | 97.4       | –                 | –                | –              | –                      |
| Ali & Na‘aya [49]             | 100        | –                 | –                | –              | –                      |
| Kebede et al [52]             | 99.0       | –                 | –                | –              | –                      |
| Onyenekwe [53]                |            |                   |                  |                |                        |
| Jaja & Yarhere [54]           | 100        | –                 | –                | –              | –                      |
| Ajibare [55]                  | 100        | –                 | –                | –              | –                      |
| Dianadji [56]                 | 97.6       | –                 | –                | –              | –                      |
| Ekpebegh et al [57]           | 73.8       | –                 | –                | 33             | –                      |
| Balde et al [58]              | 49.0       | –                 | –                | –              | –                      |
| Diagne et al [59]             | 87.0       | –                 | –                | –              | –                      |
| Edo et al [60]                | 77.1       | –                 | –                | 4.1            | –                      |
| Ogun & Adeleye [61]           | 68.6       | –                 | –                | 7.0            | –                      |
| Sarr et al [62]               | 97.3       | –                 | –                | 1              | –                      |
| Ackuaku-Dogbe et al [63]      | 67.5       | –                 | –                | –              | –                      |
| Boiro et al                   | 91.1       | –                 | –                | –              | –                      |
| Debebe et al [64]             | 94.1       | –                 | –                | –              | –                      |
| Anakwue [65]                  | 52.0       | –                 | –                | –              | –                      |
| Azagogh-Kouadio et al [67]    | 81.5       | 37.0              | –                | –              | 3.7                    |
| Darouassi et al [68]          | 52.0       | –                 | –                | –              | –                      |
| Diedhiou et al [69]           | 89.9       | –                 | –                | –              | –                      |
| Sarfo-Kantanka et al [71]     | 82.0       | 54.0              | 64.0             | –              | 4.0                    |
| Gebreoyohannes et al [72]     | –          | –                 | 37.4             | –              | –                      |
| Okafor et al [20]             | 81.0       | –                 | 54.0             | –              | –                      |
| Toyib et al [77]              | 100.0      | –                 | –                | –              | –                      |
| Boundia et al [80]            | 96.1       | –                 | –                | –              | –                      |
| Ensumo et al [82]             | 82.9       | –                 | –                | –              | –                      |
| Mariko et al [83]             | 77.1       | –                 | –                | –              | –                      |
| Mohammed [84]                 | 65.4       | –                 | –                | –              | –                      |
| Abera et al [85]              | 93.0       | –                 | –                | –              | –                      |
| Docrat et al [86]             | –          | –                 | –                | –              | 4.0                    |
| Kiffe et al [87]              | –          | –                 | –                | –              | 0.9                    |
| Maldey et al [88]             | 49.7       | –                 | 41.9             | –              | –                      |
| Mendes [89]                   | 96.0       | 16.0              | –                | –              | –                      |
| Ruto [90]                     | 76.6       | –                 | –                | –              | –                      |
| Balde et al [92]              | 94.0       | 62.0              | 91.0             | –              | 28.0                   |
| Study                                  | Tachycardia (%) | Atrial fibrillation (%) | Hand tremors (%) | Proximal myopathy (%) |
|----------------------------------------|-----------------|-------------------------|-----------------|------------------------|
| Olurin [36]                            | 93.0            | –                       | 59.0            | –                      |
| Abdulkadir et al [37]                  | 100             | –                       | 89.1            | –                      |
| Niaiara et al [39]                     | –               | 40.0                    | –               | –                      |
| Sigilai [41]                           | 55.0            | 11.0                    | 12.0            | –                      |
| Mohammed [42]                          | 44.8            | 1.7                     | 24.0            | –                      |
| Osime & Okobia [43]                    | 80.0            | –                       | 50.0            | –                      |
| Chuhwak & Obekpe [44]                  | 42.0            | –                       | 52.0            | –                      |
| Ogbera et al [45]                      | –               | 6.8                     | –               | –                      |
| Ogbera et al [46]                      | –               | 14.0                    | –               | –                      |
| Okosime et al [47]                     | –               | 2.9                     | –               | –                      |
| Sidibe et al [48]                      | 78.9            | –                       | –               | –                      |
| Ali & Naa’aya [49]                     | –               | –                       | 32.6            | –                      |
| Hattaoui et al [50]                    | –               | 61.1                    | –               | –                      |
| Ali et al [51]                         | –               | –                       | 100.0           | –                      |
| Onyenekwe [53]                         | –               | 6.9                     | 62.2            | 10.9                   |
| Ajibare [55]                           | 42.6            | 10.7                    | –               | –                      |
| Dionadjy [56]                          | 91.2            | –                       | 71.2            | 64.0                   |
| Balde et al [58]                       | 76.0            | –                       | 77.0            | –                      |
| Ogun & Adeleye [61]                    | –               | –                       | 60.9            | –                      |
| Sarr et al [62]                        | –               | –                       | 69.4            | 29                     |
| Boiro et al                            | 92.4            | –                       | –               | –                      |
| Debebe et al [64]                      | 49.0            | –                       | –               | –                      |
| Anakwue [65]                           | –               | –                       | 42.0            | –                      |
| Azagoh-Kouadio et al [67]              | 100.0           | –                       | 44.0            | –                      |
| Darouassi et al [68]                   | 78.3            | –                       | 21.3            | –                      |
| Diedhiou et al [69]                    | 50.1            | –                       | –               | –                      |
| El-Shareif [70]                        | –               | 2.8                     | 64.8            | –                      |
| Sarfo-Kantanka et al [71]              | 70.0            | 10.0                    | –               | 48.0                   |
| Gebreyohannes et al [72]               | 39.8            | –                       | 6.6             | –                      |
| Isah [73]                              | 40.5            | 2.3                     | 19.0            | –                      |
| Mohammed & Hassanein [74]              | 46.6            | –                       | –               | –                      |
| Mulatu [75]                            | –               | 11.0                    | –               | –                      |
| Toyib et al [77]                       | 100             | –                       | 100             | –                      |
| Yazidi et al [78]                      | –               | 6.1                     | –               | –                      |
| Adeleye et al [79]                     | –               | –                       | 100             | –                      |
| Demba et al [81]                       | 100             | –                       | 38.1            | –                      |
| Ersumo et al [82]                      | 42.4            | –                       | –               | –                      |
| Mariko et al [83]                      | 88.6            | –                       | –               | –                      |
| Mohammed [84]                          | 34.6            | –                       | 5.0             | –                      |
| Abera et al [85]                       | 43.0            | –                       | 17.5            | –                      |
| Docrat et al [86]                      | –               | 10.0                    | –               | 8.0                    |
| Kiffle et al [87]                      | 17.5            | –                       | 14.2            | –                      |
| Maldey et al [88]                      | –               | –                       | 50.2            | –                      |
| Mendes [89]                            | 27.0            | –                       | 33.0            | 30.0                   |
| Sylla et al [91]                       | 78.3            | –                       | 21.3            | –                      |
| Balde et al [92]                       | 92.0            | –                       | 83.0            | –                      |
| Study                                | Exophthalmos (%) | Lid retraction (%) | Lid lag (%) | Other eye signs (%) |
|--------------------------------------|------------------|--------------------|-------------|-------------------|
| Olurin [36]                          | 70.0             | 51.4               | –           | –                 |
| Abdulkadir et al [37]                | 59.1             | –                  | –           | –                 |
| Sigilai [41]                         | 40.0             | –                  | 24.0        | 53.0              |
| Mohammed [42]                        | 64.0             | –                  | 13.0        | –                 |
| Osme & Okobia [43]                   | –                | –                  | –           | 24.0              |
| Ogbera et al [45]                    | 22.0             | –                  | –           | –                 |
| Ogbera et al [46]                    | –                | –                  | –           | 38.0              |
| Okosime et al [47]                   | –                | –                  | –           | 55.0              |
| Sidibe et al [48]                    | 81.5             | –                  | –           | –                 |
| Ali et al [51]                       | –                | –                  | –           | 37.2              |
| Onyenekwe [53]                       | –                | –                  | –           | 54.7              |
| Jaja & Yarhere [54]                  | 80.0             | –                  | –           | –                 |
| Dionadji [56]                        | 38.4             | –                  | –           | –                 |
| Ekpebegh et al [57]                  | 50.0             | –                  | –           | –                 |
| Balde et al [58]                     | 26.5             | –                  | –           | –                 |
| Diagne et al [59]                    | 78.7             | –                  | –           | –                 |
| Edo et al [60]                       | –                | –                  | –           | 34.4              |
| Ogun & Adeleye [61]                  | –                | –                  | –           | 63.0              |
| Sarr et al [62]                      | 65.9             | –                  | –           | –                 |
| Ackuaku-Dogbe et al [63]             | 65.0             | –                  | –           | –                 |
| Debebe et al [64]                    | –                | 5.9                | 5.9         | –                 |
| Anakwue [65]                         | 40.0             | –                  | –           | –                 |
| Ayandipo [66]                        | –                | –                  | –           | 74.0              |
| Azagoh-Kouadio et al [67]            | 85.0             | 3.7                | –           | –                 |
| Darouassi et al [68]                 | 6.4              | –                  | –           | –                 |
| Diedhiou et al [69]                  | 72.9             | –                  | –           | –                 |
| El-Shareif [70]                      | 37.9             | –                  | –           | –                 |
| Sarfo-Kantanka et al [71]            | –                | 78.0               | 78.0        | 76.0              |
| Gebreyohannes et al [72]             | 1.9              | 0.47               | –           | –                 |
| Isah [73]                            | –                | –                  | –           | 15.6              |
| Okafor et al [20]                    | –                | –                  | –           | 75.0              |
| Toyib et al [77]                     | 87.9             | –                  | –           | –                 |
| Adeleye et al [79]                   | –                | –                  | –           | 50.0              |
| Boundia et al [80]                   | 70.7             | –                  | –           | –                 |
| Demba et al [81]                     | 43.3             | –                  | –           | –                 |
| Ersumo et al [82]                    | 2.9              | –                  | –           | –                 |
| Mariko et al [83]                    | 70.0             | 51.4               | –           | –                 |
| Mohammed [84]                        | 13.8             | –                  | –           | –                 |
| Abera et al [85]                     | 35.0             | 0.5                | 1.0         | –                 |
| Docrat et al [86]                    | –                | –                  | –           | 20.0              |
| Kiffle et al [87]                    | –                | 19.0               | 2.4         | –                 |
| Mendes [89]                          | 79.0             | –                  | 15.8        | 63.3              |
| Sylla et al [91]                     | 6.8              | –                  | –           | –                 |
| Balde et al [92]                     | 67.0             | –                  | –           | –                 |
### Table 10  Associated cardiometabolic morbidities

| Study                  | Hypertension (%) | Thyrotoxic heart disease (%) | Heart failure (%) | Diabetes (%) |
|------------------------|------------------|------------------------------|-------------------|--------------|
| Niakara et al [39]     | –                | –                            | 10.0              | –            |
| Akossou et al [40]     | –                | 46.7                         | –                 | –            |
| Sigliar [41]           | 32.0             | –                            | –                 | –            |
| Ogbera et al [45]      | 14.6             | –                            | –                 | 11.7         |
| Ogbera et al [46]      | 41.2             | –                            | –                 | 17.0         |
| Okosime et al [47]     | –                | –                            | –                 | 8.7          |
| Hattaoui et al [50]    | –                | 16.6                         | –                 | 7.5          |
| Ali et al [51]         | –                | –                            | –                 | 6.4          |
| Onyenekwe [53]         | –                | –                            | –                 | 9.7          |
| Ajibare [55]           | 81.5             | –                            | –                 | 6.4          |
| Diagne et al [59]      | –                | –                            | –                 | 11.1         |
| Edo et al [60]         | –                | –                            | –                 | 5.7          |
| Sarr et al [62]        | 17.1             | –                            | –                 | 5.1          |
| Debebe et al [64]      | 9.8              | –                            | –                 | –            |
| Diedhiou et al [69]    | –                | –                            | –                 | 6.9          |
| Isah [73]              | 30.9             | –                            | –                 | 10.1         |
| Mohammed & Hassanein [74]| 42.4           | –                            | –                 | 36.6         |
| Mulatu [75]            | 48.6             | 46.6                         | 4.1               | 8.2          |
| Okafor et al [20]      | 34.0             | –                            | –                 | –            |
| Toyib et al [77]       | –                | –                            | –                 | –            |
| Yazidi et al [78]      | –                | 6.5                          | 2.0               | –            |
| Demba et al [81]       | 20.5             | 9.4                          | –                 | 4.0          |
| Ersumo et al [82]      | 10.4             | –                            | –                 | 6.1          |
| Mohammed [84]          | 1.9              | –                            | –                 | –            |
| Kiffle et al [87]      | 2.8              | –                            | –                 | –            |
| Balde et al [92]       | 22.0             | –                            | –                 | 8.0          |

### Table 11  The pooled frequencies of the signs of thyrotoxicosis

| Signs                             | Frequency (%) | 95% CI     | p         | I² (%) | Q statistic | LFK index  |
|-----------------------------------|---------------|------------|-----------|-------|-------------|------------|
| Goiter                            | 88            | 87–90      | <0.0001   | 97    | 1193        | −8.31      |
| Thyroid bruit                     | 39            | 25–54      | <0.0001   | 91    | 53.2        | −3.32      |
| Sweaty palms                      | 54            | 39–69      | <0.0001   | 98    | 391         | 0.93       |
| Onycholyisis                      | 40            | 24–64      | <0.0001   | 99    | 97          | –          |
| Pretibial myxedema                | 7             | 4–10       | <0.0001   | 91    | 106         | 6.57       |
| Tachycardia                       | 67            | 62–70      | <0.0001   | 99    | 4361        | −8.7       |
| Atrial fibrillation               | 9             | 6–12       | <0.0001   | 88    | 113         | 4.38       |
| Hand tremor                       | 49            | 41–58      | <0.0001   | 100   | 12,036      | −8.88      |
| Proximal myopathy                 | 29            | 15–46      | <0.0001   | 97    | 181         | 0.59       |
| Exophthalmos                      | 49            | 36–41      | <0.0001   | 99    | 2085        | −1.67      |
| Lid retraction                     | 19            | 1–48       | <0.0001   | 99    | 515         | 0.2        |
| Lid lag                           | 17            | 0–43       | <0.0001   | 99    | 407         | 0.01       |
| Other eye signs                   | 49            | 35–62      | <0.0001   | 97    | 454         | −0.38      |
Fig. 11 Forest plots showing the frequencies of goiter
Fig. 12  Forest plots showing the frequencies of pretibial myxedema

Fig. 13  Forest plots showing the frequencies of tachycardia
Fig. 14 Forest plots showing the frequencies of atrial fibrillation
Fig. 15  Forest plots showing the frequencies of exophthalmos
Fig. 16 Doi plot for goiter

Fig. 17 Doi plot for pretibial myxedema
Fig. 18 Doi plot for tachycardia

Fig. 19 Doi plot for atrial fibrillation
Fig. 20  Doi plot for exophthalmos

Fig. 21  Signs of thyrotoxicosis among Africans
Strength of the study
The scope of the study is wide and the selected studies cut across all the regions of Africa which make the findings representative enough. Also, this is the first systematic review and meta-analysis, known to the authors, that has discussed the clinical characteristics of thyrotoxicosis in Africa. It is believed that the study will help to reduce delayed diagnosis and misdiagnosis of thyrotoxicosis in Africa.

Limitations
Many African countries are not English-speaking so there is a reasonable possibility that some studies on the subject matter might have been omitted thereby introducing some degree of bias. Some of the selected studies are not detailed enough as far as clinical presentation of thyrotoxicosis is concerned.

Conclusion
Thyrotoxicosis is fairly common in Africa and it has a wide range of clinical manifestations. Physicians in Africa need to pay attention to these clinical features so as to avoid delayed diagnosis or misdiagnosis of the disease.

Authors’ contributions
TAA contributed to the conception, data collation, writing and editing of the manuscript. TAA (second author) contributed to the writing and editing of the manuscript. MA contributed to the writing and editing of the manuscript. All author(s) read and approved the final manuscript.

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Author details
1 Department of Medicine, Reddington Multi-Specialist Hospital, Lagos, Nigeria. 2 Department of Medicine, Obafemi Awolowo University Teaching Hospital Complex, Ile-Ife, Nigeria. 3 Department of Medicine, Cumberland Infirmary, Carlisle, England, UK.

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Fig. 22 Pooled frequencies of cardiometabolic morbidities in thyrotoxicosis patients
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