

REVIEW

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Reported prevalence and comparison of diagnostic approaches for *Candida africana*: a systematic review with meta-analysis

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Abstract

This systematic review and meta-analysis evaluated reported prevalence and diagnostic methods for identifying *Candida africana*, an opportunistic yeast associated with vaginal and oral candidiasis. A comprehensive literature search yielded 53 studies meeting the inclusion criteria, 2 of which were case studies. The pooled prevalence of *C. africana* among 20,571 participants was 0.9% (95% CI: 0.7–1.3%), with significant heterogeneity observed ($I^2=79\%$, $p<0.01$). Subgroup analyses revealed regional variations, with North America showing the highest prevalence (4.6%, 95% CI: 1.8–11.2%). The majority 84.52% of the *C. africana* have been isolated from vaginal samples, 8.37% from oral samples, 3.77% from urine, 2.09% from glans penis swabs, and 0.42% from rectal swabs, nasal swabs, and respiratory tract expectorations respectively. No *C. africana* has been isolated from nail samples. Hyphal wall protein 1 gene PCR was the most used diagnostic method for identifying *C. africana*. It has been used to identify 70% of the isolates. A comparison of methods revealed that the Vitek-2 system consistently failed to differentiate *C. africana* from *Candida albicans*, whereas MALDI-TOF misidentified several isolates compared with HWP1 PCR. Factors beyond diagnostic methodology may influence *C. africana* detection rates. We highlight the importance of adapting molecular methods for resource-limited settings or developing equally accurate but more accessible alternatives for the identification and differentiation of highly similar and cryptic *Candida* species such as *C. africana*.

Keywords *C. africana*, Hyphal wall protein, MALDI-TOF, Vitek-2 ID system

Introduction

Candida africana is a relatively recently discovered opportunistic yeast that is associated with vaginal and oral candidiasis [1]. Experiments leading to the discovery of the *C. africana* strain began in 1993 when Tietz et al.

(1995) [2] obtained 29 vaginal isolates from females in Madagascar and Angola that displayed distinct morphological and biochemical characteristics compared with those of strains of *Candida albicans*. Currently, conventional methods for identifying yeast at the species level rely on morphological characteristics and several biochemical tests. Carbohydrate assimilation systems such as the ID 32C system are readily available for biotyping of *C. albicans*, the most common cause of vaginal candidiasis. Studies prior to 1995 [3, 4] used the ID32C and ID20C systems and reported that most *C. albicans* isolates belong to a single physiological biotype, B1, which is characterized by the assimilation of xylose, adonitol, xylitol, sorbitol, methyl-D-glucoside, N-acetyl-D-glucosamine, sucrose, and trehalose. However, they were

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unable to assimilate glycerol, L-arabinose, or melezitose. Owing to variations in the results of biochemical tests, ID systems have failed to identify cryptic species. However, despite this limitation, the assimilation of the amino sugars glucosamine (GlcN) and N-acetylglucosamine (GlcNAc) is considered invariable features of all *C. albicans* isolates [2]. In 2001, after Fourier transform infrared spectroscopy was used to demonstrate that these atypical *Candida* isolates were a monophyletic group distinct from *C. albicans* and *Candida dubliniensis*, it was suggested that this group of isolates constituted a new species within the genus *Candida*. The strain was named *C. africana* on the basis of the region where the first strains were isolated [5]. Since 2001, *C. africana* vaginitis has been reported in Africa, Europe, Asia, and the Americas, with urogenital specimens being the most common source of isolation [6]. Phenotypic chromogenic appearance on CHROMagar, sugar assimilation biochemical tests, chlamydospore production tests on corn meal agar, hyphal wall protein 1 gene polymorphism, sequencing of the internal transcribed spacer (ITS) region, particularly the ITS2 region, multilocus sequence typing (MLST), and spectrometry have been used to characterize *C. africana*. However, the accuracy and cost-effectiveness of Vitek-2-system, MALDI-TOF, and other biochemical tests commonly used in low-resource settings have not been evaluated for the identification of *C. africana*. The use of less accurate methods could lead to continued misidentification of *C. albicans* complex species, underreporting

of *C. africana* and mismanagement of recurring cases of candidiasis due to the *C. albicans* complex species. Therefore, this systematic review aimed to comprehensively determine the pooled population prevalence of *C. africana* and identify the diagnostic methods used to identify *C. africana* in clinical samples, with a focus on their applicability in resource-limited settings, where infrastructure constraints and training requirements present significant testing challenges.

Methodology

Study design

This systematic review with meta-analysis was conducted following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) methodology for systematic reviews. The review protocol was registered in PROSPERO (CRD42024560349).

Inclusion criteria and exclusion criteria

We included original research articles and case reports with methodological details used to isolate *C. africana*, published from 1995 to date and in the English language or for which English language translations were available. We used 1995 because the first atypical isolates within the *C. albicans* complex, which led to the identification of *C. africana* in 2001, were first identified in 1995 [2]. Studies with zero prevalence were included as long as they used PCR and/or sequencing method. We excluded studies that used previously identified isolates of *C. africana*.

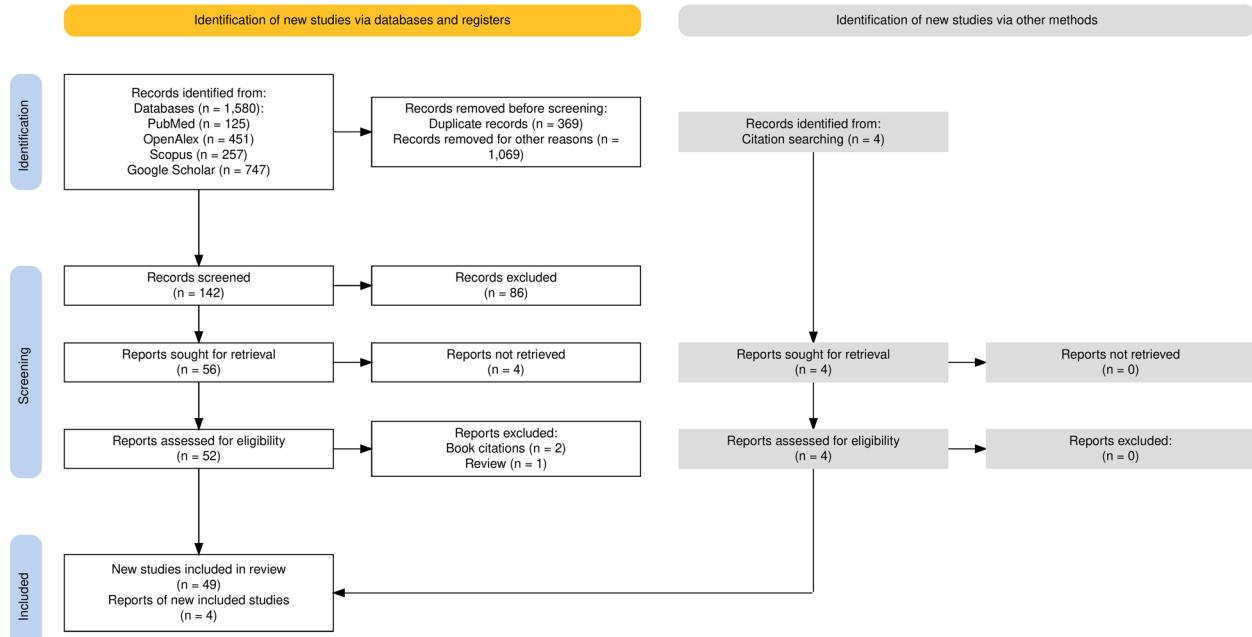


Fig. 1 PRISMA flow diagram of the included studies

Table 1 Summary of the 53 articles reporting isolation of *C. africana* included in this review

Region	Study/year	Country	Sample size	Laboratory method used	<i>C. africana</i> isolated	Sample type
South America						
	Fontecha et al., 2019 [9]	Honduras	108	Hyphal wall protein 1 gene (HWP1) PCR	2	Vaginal swab
	Mucci et al., 2017 [58]	Argentina	210	Hyphal wall protein 1 gene (HWP1) PCR	0	Vaginal swab
	Rodríguez et al., 2015 [10]	Columbia	280	MALDI-TOF	0	Vaginal swab
	Theill et al., 2016 [11]	Argentina	287	Hyphal wall protein 1 gene (HWP1) PCR	1	Vaginal swab
North America						
	Rabe et al., 2017 [59]	USA	328	Hyphal wall protein 1 gene (HWP1) PCR	23	Vaginal swab
Africa						
	Andeme et al., 2014 [12]	Gabon	355	Hyphal wall protein 1 gene (HWP1) PCR	9	Vaginal swab
	Dieng et al., 2012 [13]	Senegal	243	Hyphal wall protein 1 gene (HWP1) PCR	3	Vaginal swab
	Hana et al., 2020 [14]	Tunisia	105	Hyphal wall protein 1 gene (HWP1) PCR	1	Oral swab
	Ngouana et al., 2015 [15]	Cameroon	1354	MALDI-TOF	2	Vaginal swab
	Ngouana et al., 2019 [16]	Cameroon	402	MALDI-TOF	2	Vaginal swab
	Nnadi et al., 2012 [17]	Nigeria	320	Hyphal wall protein 1 gene (HWP1) PCR	2	Vaginal swab
	Nzenze-Afene et al., 2014 [18]	Gabon	448	Hyphal wall protein 1 gene (HWP1) PCR	4	Vaginal swab
	Pakshir et al., 2017 [19]	Egypt	110	Hyphal wall protein 1 gene (HWP1) PCR	0	Vaginal swab
	Racha et al., 2016 [20]	Algeria	55	Hyphal wall protein 1 gene (HWP1) PCR	3	Vaginal swab
	Tietz et al., 2001 [5]	Madagascar	613	Sugar assimilation tests	27	Vaginal swab
Asia						
	Anh et al., 2021 [21]	Vietnam	462	Hyphal wall protein 1 gene (HWP1) PCR	4	Vaginal swab
	Feng et al., 2015 [56]	China	252	Exon-primed intron-crossing (EPIC)-PCR	0	Nail sample
	Hu et al., 2015 [53]	China	166	Hyphal wall protein 1 gene (HWP1) PCR	5	Glans penis swab
	Lakshminpathy et al., 2023 [22]	India	53	Hyphal wall protein 1 gene (HWP1) PCR	1	Nasal Swab
	Shan et al., 2014 [23]	China	3181	Hyphal wall protein 1 gene (HWP1) PCR	15	Vaginal swab
	Sharma et al., 2014 [54]	India	283	Hyphal wall protein 1 gene (HWP1) PCR	4	Vaginal swab
Europe						
	Alonso Vargas et al., 2008 [24]	Spain	1	Hyphal wall protein 1 gene (HWP1) PCR	1	Vaginal swab
	Bigot et al., 2024 [25]	France	212	Hyphal wall protein 1 gene (HWP1) PCR	6	Vaginal swab
	Borman et al., 2013 [26]	UK	1839	Sequencing (ITS1, ITS2)	15	Vaginal swab
	Gumral et al., 2011 [57]	Turkey	195	Hyphal wall protein 1 gene (HWP1) PCR	0	Vaginal swab
	Guzel et al., 2013 [27]	Turkey	495	Sequencing (ITS1, ITS2)	0	Vaginal swab
	Hazirolan et al., 2017 [28]	Turkey	686	Hyphal wall protein 1 gene (HWP1) PCR	3	Vaginal swab
	Klesiewicz et al., 2023 [29]	Poland	326	Hyphal wall protein 1 gene (HWP1) PCR	1	Vaginal swab
	Romeo & Criseo, 2009 [30]	Italy	498	Hyphal wall protein 1 gene (HWP1) PCR	27	Vaginal swab
Middle East						
	Arastehfar et al., 2018 [31]	Iran	728	Multiplex PCR	3	Vaginal swab
	Aslani et al., 2021 [32]	Iran	350	Hyphal wall protein 1 gene (HWP1) PCR	1	Vaginal swab
	Baniasadi et al., 2022 [33]	Iran	119	Hyphal wall protein 1 gene (HWP1) PCR	3	Vaginal swab
	Diba et al., 2022 [34]	Iran	200	MALDI-TOF	1	Rectal swab
	Erfaninejad et al., 2022 [35]	Iran	276	Hyphal wall protein 1 gene (HWP1) PCR	2	Oral swab
	Fakhim et al., 2020 [36]	Iran	287	Hyphal wall protein 1 gene (HWP1) PCR	3	Vaginal swab
	Farahyar et al., 2020 [37]	Iran	330	Sequencing (ITS1, ITS2)	3	Vaginal swab
	Faridi et al., 2022 [38]	Iran	112	Hyphal wall protein 1 gene (HWP1) PCR	1	Oral swab
	Hashemi et al., 2019 [39]	Iran	260	Hyphal wall protein 1 gene (HWP1) PCR	2	Vaginal swab
	Khedri et al., 2018 [40]	Iran	150	Sequencing (ITS1, ITS2)	4	Oral swab
	Lotfali et al., 2020 [1]	Iran	2	Sequencing (ITS1, ITS2)	2	Oral swab
	Madar et al., 2024 [41]	Yemen	310	Sugar assimilation tests	3	Oral swab
	Majdabadi et al., 2018 [42]	Iran	200	Hyphal wall protein 1 gene (HWP1) PCR	2	Vaginal swab
	Makiia et al., 2020 [43]	Iraq	29	Sequencing (ITS1, ITS2)	3	Oral swab

Table 1 (continued)

Region	Study/year	Country	Sample size	Laboratory method used	<i>C. africana</i> isolated	Sample type
	Naeim et al., 2018 [55]	Iran	750	Hyphal wall protein 1 gene (HWP1) PCR	10	Vaginal swab
	Nikmanesh et al., 2020 [44]	Iran	150	Sequencing (ITS1, ITS2)	8	Urine
	Rezazadeh et al., 2016 [45]	Iran	150	Hyphal wall protein 1 gene (HWP1) PCR	4	Vaginal swab
	Roudbary et al., 2017 [46]	Iran	89	Hyphal wall protein 1 gene (HWP1) PCR	4	Oral swab
	Salehipour et al., 2021 [47]	Iran	235	Hyphal wall protein 1 gene (HWP1) PCR	1	Urine
	Sharifinia et al., 2016 [48]	Iran	121	Hyphal wall protein 1 gene (HWP1) PCR	1	Respiratory sample
	Shokohi et al., 2018 [49]	Iran	1200	Hyphal wall protein 1 gene (HWP1) PCR	1	Vaginal swab
	Shokohi et al., 2021 [50]	Iran	295	Hyphal wall protein 1 gene (HWP1) PCR	11	Vaginal swab
	Solimani et al., 2014 [51]	Iran	42	Sequencing (ITS1, ITS2)	0	Respiratory sample
	Yazdanparast et al., 2015 [52]	Iran	322	Hyphal wall protein 1 gene (HWP1) PCR	5	Vaginal swab

to study their biochemical and genetic properties and studies whose full texts could not be accessed.

the study had to demonstrate the sample types used and the laboratory methods used to isolate and report *C. africana*.

The search strategy

On 6th July 2024, three reviewers, J. B., K. C. E., and H. R. B., conducted a literature search of the PubMed, Scopus, OpenAlex, and Google Scholar databases to identify articles on *C. africana*, published between January 1, 1995, and 30th June 2024. We used the search string ("Candida africana"[all] OR "candida africana"[all]) OR *C. africana*[all] OR (HWP1[all] AND (genes[Mesh])) for PubMed, the key terms "*Candida africana*" and *C. africana*" were used to search Scopus, "*Candida africana* fungal infection" was used in OpenAlex, and the exact phrase "*Candida africana*" anywhere in the article, from 1995 to the present, was used in Google Scholar. The Scopus database was accessed through Harzing's Publish and Perish software [7].

Study selection

All records retrieved were uploaded to Zotero citations manager (Version 6.0.36), and all duplicates were removed. Three independent reviewers, J. B., K. C. E., and H. R. B., independently screened the titles and abstracts for inclusion. The keywords "*C. africana*," "*Candida africana*," and "africana" were used to filter records across all fields and tags. The titles and abstracts of the selected studies were rescreened to determine those that were isolating *C. africana* for the first time. Following selection, the full texts of the selected studies were sought and thoroughly reviewed against the inclusion criteria. Articles that did not meet the criteria were excluded from the systematic review. The reasons for exclusion were noted. After independent screening, the reviewers discussed and agreed upon different opinions on which articles to include and exclude from the review. To be included,

Risk of bias

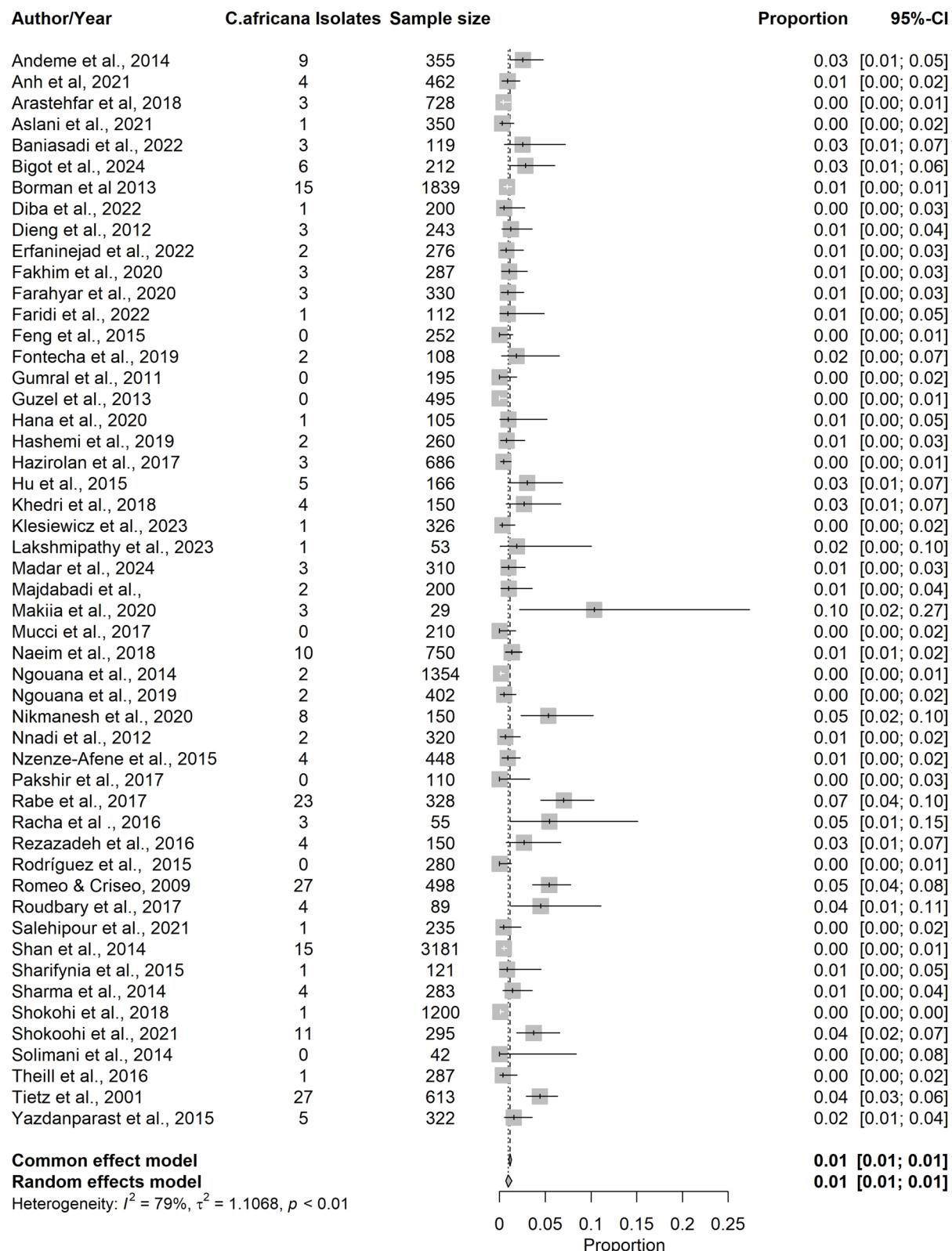
The Joanna Briggs Institute (JBI) critical appraisal tool for prevalence studies [8] was employed to systematically evaluate each study's quality and risk of bias. The studies' risk of bias was classified as low, moderate, or high (Supplementary file 2).

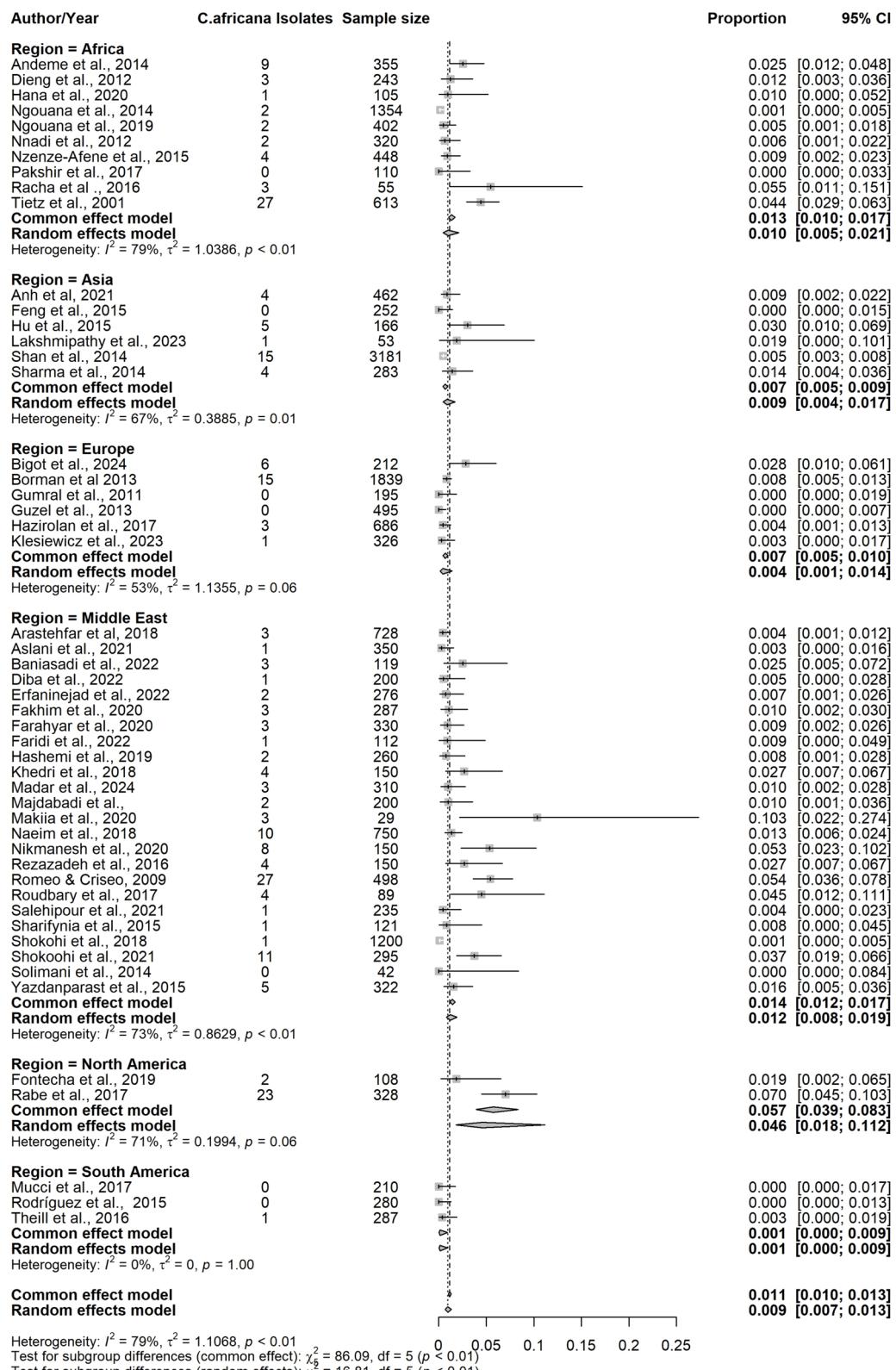
Data extraction

Three reviewers independently extracted data from the papers included in the review via an Excel data extraction form (Supplementary file 1). Specific details about the study were extracted, including the authors, publication year, country of study, study design, sample size, sample type, number of *Candida albicans* complex isolates from which *C. africana* isolates were identified, diagnostic methods, if any, used for the initial identification of *C. africana*, and reference diagnostic methods used to confirm *C. africana* isolates. The extracted data were further double checked by GM for accuracy.

Data analysis

The extracted data were cleaned, validated using Microsoft® Excel® 2019 MSO (Version 2406), and then exported to R (version 4.4.1) for analysis using the meta-package. We summarized the number of *C. africana* isolates from various studies on the basis of the diagnostic method used and determined the proportions that were identified by each method. For studies that compared two methods, we descriptively compared how effective each was at differentiating *C. africana* from *C. albicans*. Common effects and random effects models were applied to conduct a meta-analysis to evaluate the effects of diagnostic methods on the pooled prevalence of *C. africana*.

**Fig. 2** Overall prevalence of *C. africana* among the participants in 51 studies

**Fig. 3** Subgroup analysis showing the pooled prevalence of *C. africana* by geographical region across the 51 studies

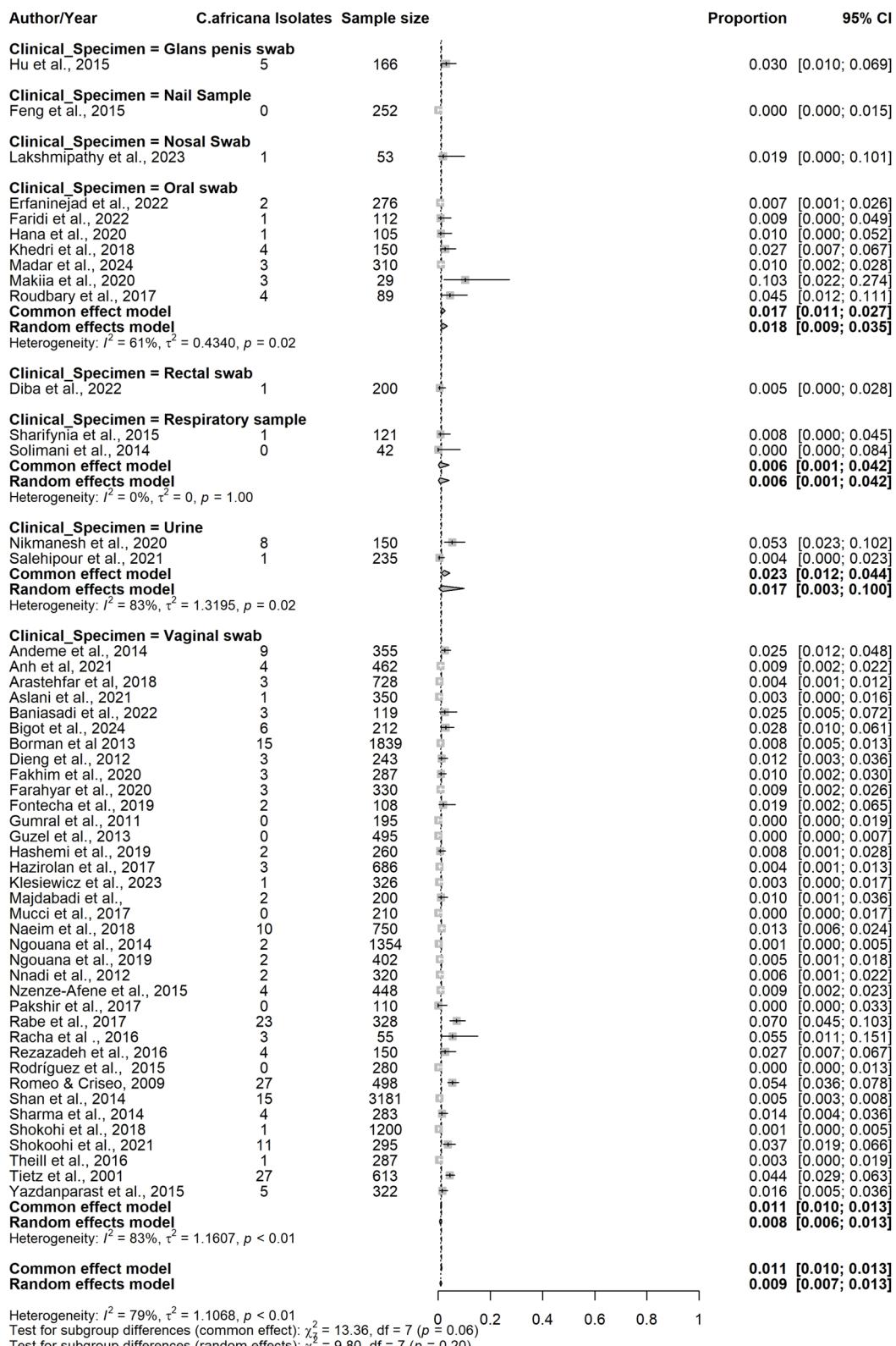
**Fig. 4** Subgroup analysis showing the pooled prevalence of *C. africana* by type of clinical specimen used across the 51 studies

Table 2 Distribution of laboratory diagnostic methods used for the identification of *C. africana* isolates

Laboratory diagnostic method	<i>C. africana</i> isolated	Proportion
Hyphal wall protein 1 gene (HWP1) PCR	165	70%
MALDI-TOF	5	2%
Multiplex PCR	3	1%
Sequencing (ITS1, ITS2)	33	14%
Sugar assimilation tests	30	13%
Grand total	236	100%

Other subgroup meta-analyses were performed using the sample type and geographical region. Heterogeneity across studies was assessed and reported as I^2 and τ^2 . Egger's test for small study effects and funnel plots were used to assess publication bias, whereas trim-and-fill analysis was used to adjust for publication bias. Effect sizes were calculated as proportions with 95% confidence intervals for individual studies, and statistical significance was set at $p < 0.05$ for all analyses.

Results

Search results

We found 1580 records from the database searches. After removing duplicated articles, we screened 142 records, from which we reviewed 52 full-text documents and ultimately included 49 papers [1, 5, 9–55], as shown in Fig. 1. Four records [56–59] were accessed by searching the references of the included studies.

Study characteristics

We included 53 studies from the Middle East, Africa, North America, South America, and Asia, as shown in Table 1. All 53 studies were used to compute the proportion of *C. africana* isolates that were detected using various diagnostic methods. Two case studies [1, 24] were excluded from the meta-analysis.

Pooled population prevalence of *C. africana*

This meta-analysis included 51 studies with a total population size of 20,571. The overall pooled population prevalence of *C. africana* was 0.9% (95% CI: 0.7–1.3%) based on random effects models (Fig. 2), with significant heterogeneity observed across studies ($I^2 = 79\%$, $p < 0.01$). In terms of geographical region, Fig. 3, and using the random effects model, North America had the highest prevalence, at 4.6% (95% CI 1.8–11.2), followed by the Middle East at 1.2% (95% CI, 0.8–1.9%) and Africa at 1.0% (95% CI 0.5–2.1%). Despite the regional variation in the prevalence rates of *C. africana*, confidence intervals overlapped between Africa, Asia, Europe, and the

Middle East. Subgroup analyses conducted by sample type (Fig. 4) revealed that studies that used oral samples (1.8%, 95% CI 0.9–3.5%) and urine samples (1.7%, 95% CI 0.3–10.0) had the highest pooled prevalence. However, 201 out of the 236 *C. africana* isolates were isolated from vaginal specimens. Other samples that have been used to isolate *C. africana* include rectal, urine, and nasal samples.

Laboratory methods used for the identification of *C. africana*

Hyphal wall protein 1 gene size polymorphism is the most used method for the isolation of *C. africana*, identifying 70% of the 236 total isolates, as shown in Table 2. Other methods that have been used include sequencing (ITS1, ITS2), sugar assimilation tests, matrix-assisted laser desorption and ionization-time-of-flight mass spectrometry (MALDI-TOF), and multiplex PCR.

A subgroup meta-analysis based on diagnostic methods, Fig. 5, reached statistical significance in both the common effect ($\chi^2 = 46.66$, $df = 5$, $p < 0.01$) and random effects ($\chi^2 = 15.66$, $df = 5$, $p < 0.01$) models, suggesting that the choice of diagnostic technology significantly influenced the reported prevalence of *C. africana*. However, the overall heterogeneity remained high ($I^2 = 79\%$, $\tau^2 = 1.1068$, $p < 0.01$), even after accounting for differences in diagnostic methods. This persistent heterogeneity could be due to factors such as host genetic factors, lifestyle, nutrition/diet, environmental conditions, study designs, testing infrastructures available, and the prevalence of *C. africana* in the study settings.

Comparison of diagnostic methods used to identify *C. africana* from clinical specimens

Four studies used both the Vitek-2 system and PCR for the differentiation of *C. africana* from the *C. albicans* complex Table 3. Notably, the Vitek-2 ID system consistently failed to identify any *C. africana* isolates in all four studies, which were later detected by HWP1 PCR method. This high false negativity rate (100%) across all studies highlights the significant inability of the Vitek-2 system to distinguish *C. africana* from *C. albicans*. Compared with HWP1 PCR, MALDI-TOF misidentified a total of five *C. africana* isolates in three different studies. However, when used alone, MALDI-TOF correctly identified *C. africana* from the rectal and vaginal samples. API *Candida* system, ID 32C system, and PCR-RFLP of ITS all failed to differentiate *C. africana* from *C. albicans*. Noteworthy, HWP1 PCR misidentified six *C. africana* that were later correctly identified by sequencing of ITS1 and ITS2 regions.

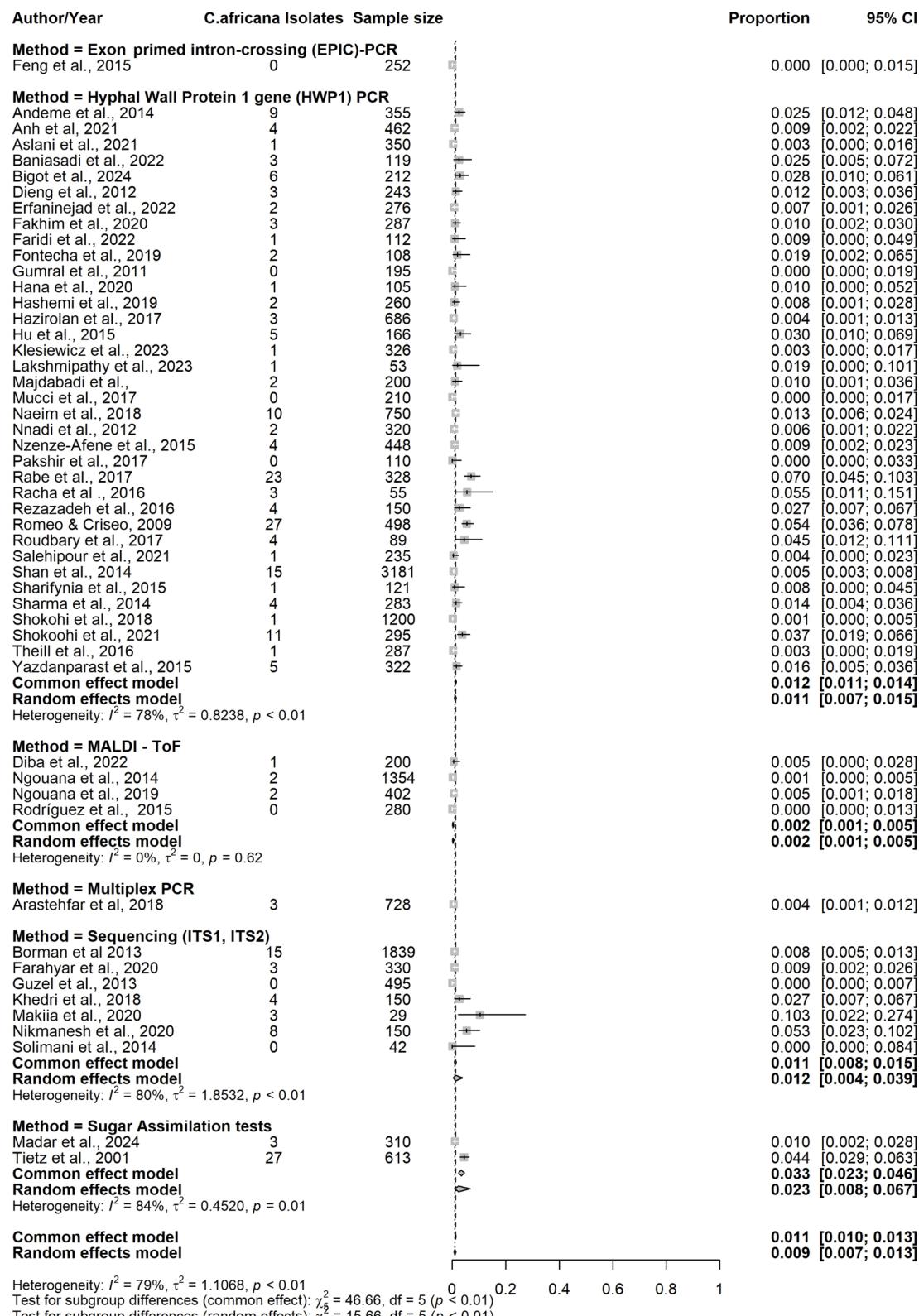
**Fig. 5** Subgroup analysis showing the pooled prevalence of *C. africana* by diagnostic method across the studies

Table 3 Comparison of the Vitek-2 system and MALDI-TOF with HWP1 PCR for the identification of *C. africana*

Authors/year	Sample size	Test method	<i>C. africana</i> isolates	Reference method	<i>C. africana</i> isolates
Shan et al., 2014 [23]	1014	API <i>Candida</i> system	0	HWP1 PCR	15
Farahyar et al., 2020 [37]	100	HWP1 PCR	3	Sequencing (ITS1, ITS2)	3
Hazirolan et al., 2017 [28]	376	HWP1 PCR	3	Sequencing (ITS1, ITS2)	3
Lotfali et al., 2020 [1]	2	HWP1 PCR	2	Sequencing (ITS1, ITS2)	2
Nikmanesh et al., 2020 [44]	150	HWP1 PCR	2	Sequencing (ITS1, ITS2)	8
Theill et al., 2016 [11]	287	HWP1 PCR	1	Sequencing (ITS1, ITS2)	1
Alonso Vargas et al., 2008 [24]	1	ID32C system	0	HWP1 PCR	1
Hazirolan et al., 2017 [28]	376	ID32C system	0	HWP1 PCR	3
Ngouana et al., 2015 [15]	115	ID32C system	0	MALDI-TF	2
Hazirolan et al., 2017 [28]	376	MALDI-TOF	0	HWP1 PCR	3
Klesiewicz et al., 2023 [29]	326	MALDI-TOF	0	HWP1 PCR	1
Salehipour et al., 2021 [47]	235	MALDI-TOF	0	HWP1 PCR	1
Fontecha et al., 2019 [9]	66	PCR-RFLP of ITS	0	HWP1 PCR	2
Naeim et al., 2018 [55]	119	PCR-RFLP of ITS	0	HWP1 PCR	10
Rezazadeh et al., 2016 [45]	67	PCR-RFLP of ITS	0	HWP1 PCR	4
Sharifynia et al., 2016 [48]	83	PCR-RFLP of ITS	0	HWP1 PCR	1
Shokoohi et al., 2021 [50]	133	PCR-RFLP of ITS	0	HWP1 PCR	11
Hana et al., 2020 [14]	66	Vitek-2 ID system	0	HWP1 PCR	1
Klesiewicz et al., 2023 [29]	326	Vitek-2 ID system	0	HWP1 PCR	1
Orazio Romeo & Giuseppe Criseo, 2009 [30]	376	Vitek-2 ID system	0	HWP1 PCR	27
Sharma et al., 2014 [54]	279	Vitek-2 ID system	0	HWP1 PCR	4

Risk of publication bias

There was significant publication bias both visually, Fig. 6, and using the Egger's test ($t = -4.79$, $df=49$, $p\text{-value}=0.0$). When trim-and-fill analysis was used to adjust for publication bias by imputing studies, the adjusted pooled proportion increased to 2.72% (95% CI 1.86–3.97%) (Fig. 7).

Risk of bias

All the 53 studies included in this review had a low risk of bias as shown in supplementary material 2.

Discussion

We provide a comprehensive evaluation of the prevalence and diagnostic methods for *C. africana*, a recently identified opportunistic yeast within the *C. albicans* complex. Our findings revealed a pooled population prevalence of 0.9% (95% CI: 0.7–1.3%), with significant heterogeneity observed across studies ($I^2=79\%$, $p<0.01$). This heterogeneity suggests that factors beyond diagnostic methodology may influence *C. africana* detection rates, including geographical variation, patient demographics, and study design elements. The regional variation in *C. africana* prevalence could be attributed to

differences in testing practices, healthcare infrastructure, or genuine epidemiological variations. However, the overlapping confidence intervals between most regions indicate that the prevalence may generally be the same.

Our analysis of diagnostic methods highlights the superiority of molecular diagnostic techniques, particularly hyphal wall protein 1 (HWP1) gene PCR, which identified 70% of *C. africana* isolates. This is similar to the previously reported high sensitivity (98%) and specificity (>90%) of PCR methods in diagnosing invasive candidiasis [60]. The consistent failure of the Vitek-2 system to differentiate *C. africana* from *C. albicans* [29, 30, 54, 61], underscores the limitations of traditional biochemical identification methods in differentiating and identifying closely related fungal species and presents significant challenges for low-resource clinical settings. While our findings clearly demonstrate the superiority of molecular techniques, their implementation in resource-limited areas is complicated by constraints in testing infrastructure and training needs. As noted by Soriano et al. (2023) [62] in their review of current clinical challenges and unmet needs in diagnosing *Candida* infections, PCR methods are primarily used in reference laboratories, affecting the need for shorter turns around time, and

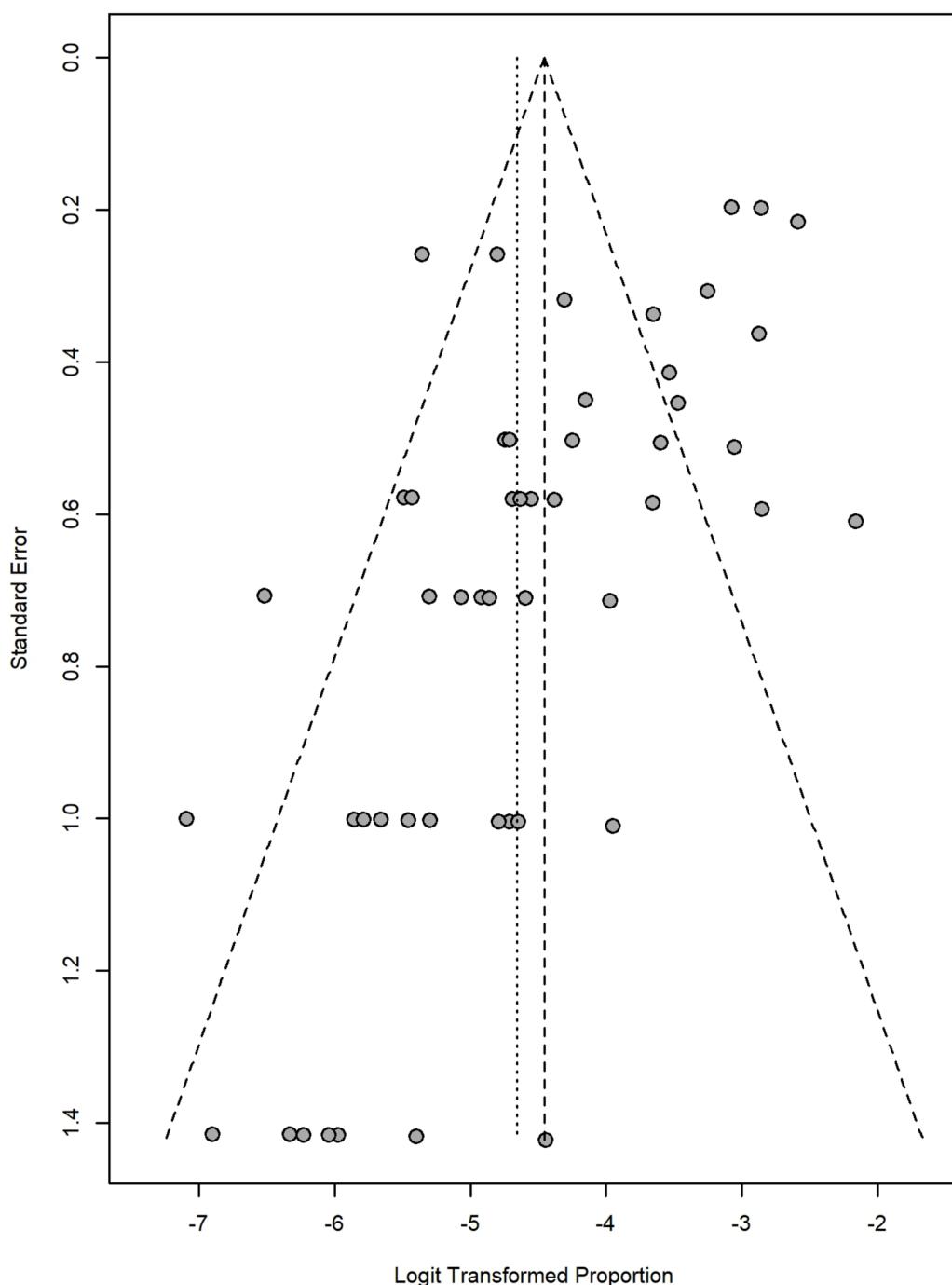


Fig. 6 A funnel plot showing publication bias across the 51 studies included in the meta-analysis

they are costly for routine testing. Additionally, many laboratories in developing countries lack the necessary equipment, reagents, and skilled personnel to perform molecular tests routinely. These gaps could lead to continued misidentification of *C. africana* in settings that rely on biochemical tests or an automated Vitek-2 identification system, potentially impacting patient care and

epidemiological understanding. The cost-effectiveness of implementing molecular methods versus the clinical impact of potential misidentification needs careful consideration. As suggested by Ondoña et al. (2020) [63], a tiered approach might be beneficial, where regional reference laboratories equipped with molecular capabilities support multiple primary healthcare

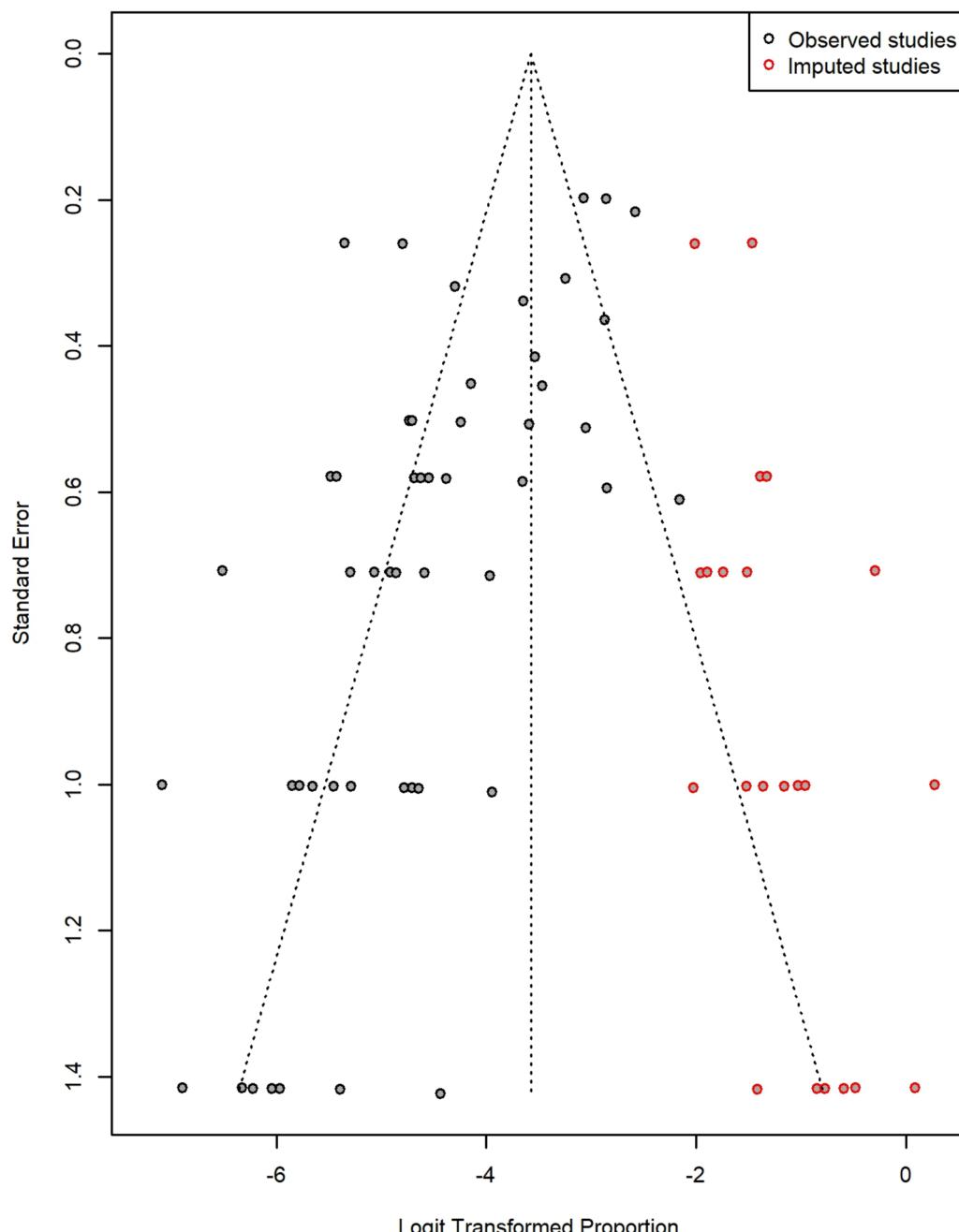


Fig. 7 A funnel plot showing trim-and-fill analysis imputing 22 studies to the right to adjust for publication bias

facilities. Alternatively, the development of simpler, more cost-effective molecular tests or improvements in the specificity of chromogenic media could bridge this gap. MALDI-TOF offers hope for replacing phenotypic methods in identifying cryptic *Candida* species, but as recommended by Bizzini et al. (2010) [64], systematic database-related taxonomical differences, the poor discrimination of the MALDI-TOF MS spectra, and a

valid extraction step must be addressed to improve the accuracy of the method.

The isolation of *C. africana* from oral and urine samples is intriguing, raising the potential of this species being involved in oral thrush and urinary tract infections. This observation warrants further investigations, as it could suggest a preference of *C. africana* for certain host niches.

The significant publication bias detected in our analysis is a limitation that must be acknowledged. The adjusted pooled proportion after trimming and filling analysis (2.72%, 95% CI: 1.86–3.97%) suggested that the true prevalence of *C. africana* may be higher than that estimated in this review. This highlights the need for more large population-based cross-sectional and observational studies using molecular methods to differentiate between closely related *Candida* species. We were unable to calculate the sensitivity and specificity of each diagnostic method due to incomplete data on true positives and false negatives. As a result, we could not determine the diagnostic accuracy for each method. Furthermore, the use of preserved clinical isolates of *C. albicans* in some studies instead of fresh clinical samples made it difficult to accurately assess the health status of the participants. This limitation prevented us from accounting for the health status of participants in our meta-analysis. Future research should focus on adapting superior methods for resource-limited settings or developing equally accurate but more accessible alternatives to ensure equitable diagnostic capabilities globally.

Conclusion

While we provide an estimated prevalence of *C. africana*, the high degree of heterogeneity, potential publication bias, and lack of significant subgroup differences suggest that factors beyond diagnostic methodology may influence *C. africana* detection rates. These factors may include geographical variation, patient demographics, or specific study design elements, warranting further investigation in future research. However, MALDI-TOF showed limitations in identifying uncommon and cryptic *C. africana* species, whereas the Vitek-2 system has been completely unable to identify *C. africana*. Even when the Vitek-2 system and biochemical tests are routine useful tools in mycology laboratories in resource-limited settings, they should not be used to differentiate highly similar *C. albicans* and *C. africana*.

Abbreviations

HWP1	Hyphal wall protein 1
MALDI-TOF	Matrix-assisted laser desorption and ionization time of flight
PCR	Polymerase chain reaction
ITS	Internal transcribed spacer
MLST	Multilocus sequence typing
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
ID	Identification
CI	Confidence interval
ID32C/ID20C	Commercial yeast identification systems
JBI	Joanna Briggs Institute
KCE	Kasule Charles Emmanuel
JB	Jonani Bwambale
HRB	Herman Roman Bwire
GM	Gerald Mboowa
EPIC	Exon-primed intron-crossing

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s41512-024-00180-6>.

Supplementary Material 1. Data extracted from the 53 studies included in this systematic review, data used for the meta-analysis, and data used to compare diagnostic methods.

Supplementary Material 2. Risk of bias assessment using the Joanna Briggs Institute checklist for prevalence studies.

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None.

Data summary

All data supporting the findings of this study are available within the paper and its supplementary information. Data extracted from articles is supplementary file 1, and evaluation of included studies for risk of bias is supplementary material II.

Authors' contributions

JB and GM conceptualized and designed the study. JB, HRB, and KCE searched for, screened, and extracted the data for thematic analysis. JB performed the analysis. JB, HRB, and KCE wrote the manuscript draft. GM reviewed the literature collection, screening, extraction processes and the manuscript for intellectual content. All the authors approved the final version of the manuscript.

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Data availability

All data supporting the findings of this study are available within the paper and its Supplementary Information.

Declarations

Ethics approval and consent to participate

This systematic review used published data and did not require ethical approval.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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