

A systematic review and meta-analysis on the prevalence of vulvovaginal candidiasis in Southeast Asian countries

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ABSTRACT

Vulvovaginal candidiasis (VVC) is a disease caused by pathogenic *Candida* species. This disease typically affects women of reproductive age with high sexual activity (i.e., sex workers), poor educational attainment and economic status, and infrequent hygiene practices. VVC remains a major public health concern. VVC prevalence across Southeast Asian countries remains poorly understood. To address this concern, the current study estimated the current prevalence of VVC infections among women in Southeast Asian countries by conducting a systematic review and meta-analyses. All studies reporting the prevalence of VVC in Southeast Asia were obtained from Ovid Medline, Scopus, and CINAHL. A review of titles and abstracts was done independently by three reviewers. The quality of the studies was assessed using the Newcastle-Ottawa scale. Meta-analysis was performed in R v.4.1.1 using the ‘meta’ package (version 4.19-0). Based on the results of the current study, the pooled estimated prevalence of VVC among Southeast Asian women is 23.0% (95% CI: 18.0% to 28.0%). Across countries, Laos had the highest estimated prevalence at 33.0% (95% CI: 22.0% to 46.0%). Subgroup analysis based on

pregnancy status and occupation revealed a higher estimated prevalence among non-pregnant women (32.0%, 95% CI: 25.0% to 40.0%) and non-sex workers (33.0%, 95% CI: 20.0% to 48.0%). Based on the diagnostic method, the prevalence was higher for the combinatorial approach using microscopy, a culture-based approach, and molecular techniques (51.0%) and lowest when solely based on clinical diagnosis (9.0%, 95% CI: 1.0% to 22.0%) or an exclusively culture-based approach (11%, 95% CI: 6.0% to 18.0%). Overall, further study is necessary to accurately characterize the current distribution of VVC across Southeast Asian countries. Developing more effective diagnostic and management strategies is to improve the health of affected women.

INTRODUCTION

Candidiasis are opportunistic yeast infections of the genus *Candida*, such as *C. albicans*, *C. auris*, *C. glabrata*, and *C. tropicalis*. Typically, *Candida* sp. Colonizes the skin, the gastrointestinal tract mucosa, and the vagina without causing infection in a healthy individual (Fidel, 2004; Fidel et al., 2004). However, in an immunocompromised state, *Candida* sp. may propagate and cause disease (Cassone, 2015; Rosati et al., 2020).

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KEYWORDS

Southeastern Asia, vulvovaginal candidiasis, health behaviors, sex work, pregnancy

Globally, vulvovaginal candidiasis (VVC) is known to infect nearly 75% of women of reproductive age at least once throughout their lifetime and has been shown to impact the quality of life of infected women (Denning et al., 2018). It manifests as fungal overgrowth in the vaginal lumen leading to excessive itchiness (i.e., vaginal pruritus), a burning or painful sensation in the urethra (i.e., dysuria), and the formation of genital ulcers or sores (Mtibaa et al., 2017). These symptoms are often accompanied by odorous vaginal discharge of epithelial slough, immune cells, yeast cells, and vaginal fluid (Ge et al., 2022; Mtibaa et al., 2017). Changes in the host's physiologic state due to pregnancy and a combination of occupational and lifestyle factors are known risk factors for VVC (Mtibaa et al., 2017; Sobel et al., 1988). Additionally, the emergence of antifungal resistance across certain strains of *Candida* sp. has also contributed to the growing incidence of infections across the region. However, studies investigating these risk factors are not conclusive and require further investigation and validation in the context of Southeast Asian countries.

Thus, in this study, the prevalence of VVC was assessed alongside the diagnostic technique utilized and clinical presentation across women from Southeast Asian countries. This study seeks to elaborate on the risk factors and burden of VVC in Southeast Asia. The study findings can help identify focal points on the epidemiology of VVC infections among susceptible Southeast Asian women.

METHODOLOGY

Protocol Design and Registration

A systematic literature review and meta-analysis of various epidemiologic cohort, case-control, and cross-sectional studies was carried out. The study protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42022313380). This review followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guide (PRISMA).

Research Question

To formulate the research question, the PECO anagram (population; exposure; comparison, and outcome) was used (Table 1). Due to the nature of this study, the comparison element was not utilized. Thus, the present study aimed to determine the prevalence of VVC across women from Southeast Asian countries and to identify the diagnostic tools, clinical manifestations, and risk factors of the disease.

Table 1: Description of the PECO strategy.

PECO Strategy	Elaboration of study strategy
Population	Women in any age group in Southeast Asia diagnosed with vulvovaginal candidiasis
Exposure	Prevalence of vulvovaginal candidiasis
Comparison	Not applicable to this study
Outcome	Vulvovaginal candidiasis

Eligibility Criteria

All original articles with reported data on the prevalence of VVC among Southeast Asian women were included in the present study. This included cross-sectional, case-control, and cohort studies in any Southeast Asian country. No time limitation or language restriction was set. Review articles, case reports, books or book chapters, letters to the editor, editorials, and case series without original data were excluded from the study. Studies wherein the prevalence of VVC was not reported were also excluded.

Sources of Information and Search Strategy

All original articles related to the PECO of the current study from OVID Medline, EBSCO CINAHL, and Scopus databases were included. The following search strategy was utilized: (TITLE-ABS-KEY ((candida OR candidosis OR candidias* OR "yeast infection") AND (vulvovagin* OR vagin* OR vulv*)) AND TITLE-ABS-KEY (thai* OR philippin* OR singapor* OR malaysi* OR indonesi* OR cambodi* OR vietnam* OR "Viet Nam" OR laos OR lao OR brunei OR "Brunei Darussalam" OR "Timor Leste" OR "East Timor" OR myanmar)).

Selection of Studies and Data Extraction

After removing duplicates, the three reviewers independently reviewed the title and abstracts. Full-text articles were retrieved for all the eligible studies and were evaluated independently by the three reviewers. All irrelevant articles were excluded, with recordkeeping of the reasons for exclusion. Data on authorship, year of publication, country of origin, diagnostic tool used to identify the disease, age of study population, sociodemographic characteristics, clinical manifestations, and the risk factors of the disease were collected and tabulated (Table 2).

Quality Assessment

The quality of the included studies was assessed using the Newcastle-Ottawa Scale (NOS) for case-control, cohort, and cross-sectional studies. The scale is composed of eight questions covering three domains: 1) selection of study groups (four points for case-control and cohort studies and five points for cross-sectional studies); 2) comparability of groups (two points); and 3) ascertainment of exposure and outcomes (three points). The scale assigns a maximum score of nine for case-control and cohort studies and a maximum score of 10 for cross-sectional studies, representing a high-quality study (Lo et al., 2014; Wells et al., 2013). Studies that score a rating of 7-9 qualify as high-quality studies, while studies that score a rating of 4-6 would be classified as moderate quality. Studies that score 1-3 would be classified as low-quality.

Data Analysis

All analyses will be done in R v.4.1.1 (R Foundation for Statistical Computing) using the 'meta' package (version 4.19-0). Summary estimates with a 95% confidence interval (CI) will be calculated. If heterogeneity exists, the random-effects model was used to estimate the pooled OR. For subgroup analyses, country variables, pregnancy status, sex worker occupation, and diagnostics were utilized. Otherwise, a fixed-effects model was used. Age was not utilized for subgroup analysis due to insufficient studies reporting an exact mean or median age of study participants.

RESULTS

Results of the Search. A total of 152 studies were extracted from OVID Medline, EBSCO CINAHL, and Scopus. After removing duplicates and screening for inclusion of keywords, eligibility, and relevance, 22 articles were compiled for review. A total of 16 studies were removed due to the absence of prevalence metrics for vulvovaginal candidiasis (Figure 1). The

study period, study site, sample size, age, reported prevalence, type of study design, clinical manifestations, risk factors, and diagnostic method used were included. Then, each article was

reviewed independently by three reviewers and assessed using the NOS.

Table 2: Articles about vulvovaginal candidiasis (VVC) in Southeast Asian countries.

#	Author(s)	Study Period		Study Site	Sample Size	Age	Prevalence (%)	95% CI	Clinical Manifestations	Risk Factors	Diagnostic Method	Study Type
		Start	End									
01	(Teoh & Ngeow, 1980)	-		Malaysia	30	Range: 23-45 years	6.7%	-	Vaginal discharge, vulvovaginal pruritus, dysuria	Prostitution	SDA culture	Cross-Sectional
02	(Cheong et al., 1992)	1987	1988	Malaysia	164	Mean: 34.0 (SD: 7.2)	25.0%	-	Vaginal discharge	-	Vaginal wet mount microscopy, Gram staining, SDA culture,	Case-Control
03					188	Median: 26 years	9.0%	-				
04	(Pillay et al., 1994)	-		Malaysia	350	Mean: 30.0 years	28.0%	-	Vaginal discharge, dysuria	Use of intrauterine contraceptive devices	Cervico-vaginal wet mount microscopy	Cross-Sectional
05	(Chandeying et al., 1998)	-		Thailand	240	Mean: 25.0 years	22.0%	-	Vaginal discharge, vulvovaginal pruritus	-	Vaginal wet mount microscopy, Gram staining, KOH test	Cohort
06	(Ruggao et al., 1998)	1992	1996	Thailand	481	Mean: 25.8 years (SD: 5.4)	7.1%	-	Vaginal discharge, genital ulcers	-	Vaginal wet mount microscopy, KOH test, Gram staining	Case-Control
07	(Kovavisarach & Kanjanahareutai, 2001)	1996	1997	Thailand	220	Mean: 34.1 years (SD: 6.8)	14.5%	-	-	Premature rupture of membrane (PROM)	Chocolate agar culture	Case-Control
08				Thailand	220	Median: 27.0 years (Range: 18-44)	7.7%	-				
09	(Reed et al., 2001)	1998		Indonesia	626	Mean: 25.7 years (SD: 4.8)	25.4%	-	Vaginal discharge, vulvovaginal pruritus, dysuria, genital ulcers	Genital cleansing	Vaginal wet mount microscopy, pH determination, SDA culture, KOH test	Cohort
10	(P. K. Anh et al., 2003)	1998		Vietnam	1000	Mean: 35.7 years (SD: 6.6)	34.2%	-	Vaginal discharge, vulvovaginal pruritus, dysuria, genital ulcers	Use of intrauterine devices	Vaginal wet mount microscopy, KOH test, Gram staining	Cross-Sectional
11	(Goto et al., 2005)	-		Vietnam	505	Mean: 27.0 years	17.0%	-	Vaginal discharge, vulvovaginal pruritus, dysuria	Use of contraceptives, low household assets, living with husband	Vaginal wet mount microscopy, Gram staining	Cross-Sectional
12	(Thammalangsy et al., 2006)	2001	2002	Laos	500	Mean: 31.2 years (SD: 7.4)	27.0%	23.1-30.9	Vaginal discharge, vulvovaginal pruritus, dysuria, dyspareunia, genital ulcers	-	Vaginal wet mount microscopy, Gram staining	Cross-Sectional

13	(Go et al., 2006)	1998	Vietnam	194	Mean: 36 years (Range: 18-49)	25.3%	19.3-32.0	Vaginal discharge, vaginal pruritus	Low education	Vaginal wet mount microscopy, Gram staining	Cross-Sectional	
14	(Klotz et al., 2007)	2005	Vietnam	125	-	2.5%	-	-	HIV	Clinical appearance, response to therapy	Cross-Sectional	
15	(Sihavong et al., 2007)	2000	2001	Laos	1125	Mean: 29 years (SD: 7.0)	39.5%	-	Vaginal discharge, vulvovaginal pruritus, dysuria, genital ulcers	-	Vaginal wet mount microscopy, Gram staining	Cross-Sectional
16	(Lan et al., 2008)	2006	Vietnam	1102	-	26.0%	-	Vaginal discharge, vulvovaginal pruritus, dysuria, genital ulcers	Vaginal douching, high education level, low economic status	Vaginal wet mount microscopy	Cross-Sectional	
17	(T. V. Nguyen et al., 2008)	2003	Vietnam	406	Mean: 17.2 years	12.2%	9.2-15.9	-	-	Vaginal wet mount microscopy	Cross-Sectional	
18	(Hng et al., 2009)	2003	2004	Vietnam	748	Range: 15-45 years	34.0%	31.2-37.1	Vaginal discharge	Abortion	Vaginal wet mount microscopy, KOH test, Gram staining, SDA culture	Cross-Sectional
19	(Masri et al., 2015)	2011	Malaysia	1163	Mean: 31.0 (SD: 5.24)	17.2%	-	-	Pregnancy	SDA culture, biochemical identification	Cross-Sectional	
20	(Asavapiriyant et al., 2016a)	2006	2007	Thailand	121	Mean: 35.5 years	19.0%	-	-	-	-	Cross-Sectional
21	(Sopian et al., 2016)	2006	2012	Malaysia	809	-	14.6%	-	Vaginal discharge, vulvovaginal pruritus	-	-	Case-Control
22	(Le et al., 2019)	2016	2017	Vietnam	597	-	17.4%	-	Vaginal discharge	-	Vaginal wet mount microscopy, Gram staining, SDA culture	Cross-Sectional
23	(D. N. Anh et al., 2021)	2019	2020	Vietnam	462	Range: 23-45 years	51.3%	31.2-37.1	-	-	-	-
24	(Q. H. V. Nguyen et al., 2021)	2017	2019	Vietnam	45	Mean: 34.0 (SD: 7.2)	64.4%	-	Vaginal discharge	-	Vaginal wet mount microscopy, Gram staining	Case-Control
25					79	Median: 26 years	64.6%	-				

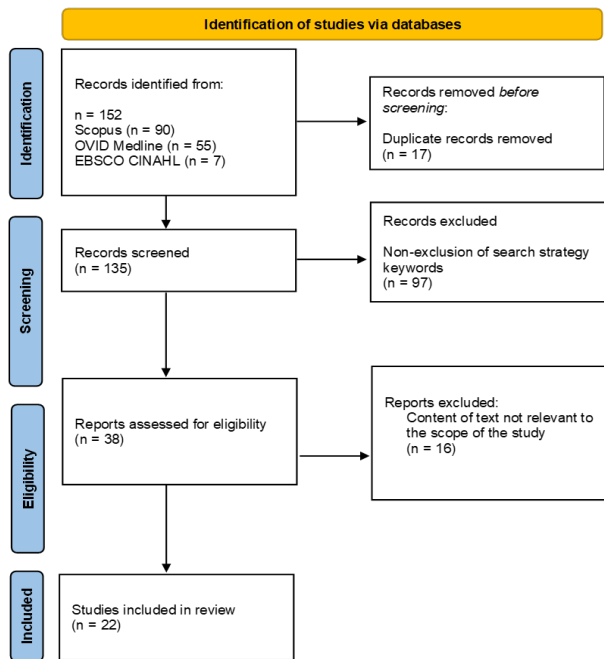


Figure 1: PRISMA flowchart showing the search and study selection strategy.

Asia. Of the 22 studies, a total of 10 studies from Vietnam, five studies from Malaysia, four studies from Thailand, two studies from Laos, and 1 study from Indonesia were identified. These served as the basis for subgroup analysis per country. In determining possible risk factors for VVC, including pregnancy and occupation, 14 and 8 studies were used. In comparing VVC prevalence across varying diagnostic methods, all 22 studies were used.

Systematic Review. A summary of the findings of each study is provided in Table 2. Generally, the participants of each study were women aged 18 to 49 years old, predominantly either pregnant women or commercial sex workers. The most common clinical manifestation of VVC reported was vaginal discharge, followed by vulvovaginal pruritus, genital ulcers, and dysuria. The vaginal wet mount was the preferred diagnostic method of choice for the diagnosis of the disease, with KOH, Gram staining, and culture methods occasionally used as confirmatory tests for the diagnosis. In terms of risk factors, these ranged from pregnancy status and associated complications, occupation, frequency of genital cleansing, use of intrauterine devices, and low educational attainment or economic status. Based on the NOS, a total of 14 of 22 studies (66.7%) were classified as high quality (NOS: 7-9), whereas seven studies (33.3%) were identified as moderate quality and only one study (4.8%) was classified as low quality (NOS: 1-3) (Table 3).

Characteristics of Studies Included. A total of 22 studies were used to determine the overall prevalence of VVC in Southeast

Table 3: Newcastle-Ottawa scoring of studies on VVC prevalence across Southeast Asian countries.

Study	Study Design	Selection	Comparability	Exposure	Overall
Teoh & Ngeow, 1980	Cross-Sectional	+	+	+	3
Cheong et al., 1992	Case-Control	+	++	+++	6
Pillay et al., 1994	Cross-Sectional	+++	+	++	6
Chandeying et al., 1998	Cohort	++++	+	+	6
Rugpao et al., 1998	Case-Control	++	++	++	6
Kovavisarach et al., 2001	Case-Control	++	++	+++	7
Reed et al., 2001	Cohort	++++	-	++	6
Anh et al., 2003	Cross-Sectional	+++	++	+++	8
Goto et al., 2005	Cross-Sectional	+++	+	+++	7
Thammalangsy et al., 2006	Cross-Sectional	+++	++	+++	8
Go et al., 2006	Cross-Sectional	+++++	+	+++	9
Klotz et al., 2007	Cross-Sectional	+++	+	+++	7
Sihavong et al., 2007	Cross-Sectional	+++	++	++	7
Lan et al., 2008	Cross-Sectional	++++	+	+++	8
Nguyen et al., 2008	Cross-Sectional	+++	+	+++	7
Hng et al., 2009	Cross-Sectional	++++	+	+++	8
Masri et al., 2015	Cross-Sectional	+++	+	++	6
Asavapiryanont et al., 2016	Cross-Sectional	+++	+	+++	7
Sopian et al., 2016	Case-Control	+++	+	+++	7
Le et al., 2019	Cross-Sectional	++++	+	+++	8

Anh et al., 2021	Cross-Sectional	+++	++	+++	8
Nguyen et al., 2021	Case-Control	++	+	+++	6

Meta-analysis. A meta-analysis was conducted based on the reported prevalence metrics from each study. Overall, there is an estimated pooled prevalence of 23.0% (CI: 18.0% to 28.0%) of VVC across Southeast Asian countries (Figure 2). Subgroup analyses on the country of origin, pregnancy status, and occupation of the studied population were also performed to reveal underlying patterns in VVC infections. Based on countries of origin, Laos had the highest estimated pooled prevalence of VVC at 33.0% (CI: 22.0% to 46.0%), followed by Vietnam at 29% (CI: 21.0% to 38.0%), then Malaysia at 17.0% (CI: 12.0% to 22.0%), and Thailand at 13.0% (CI: 8.0% to 20.0%) (Figure 3). Only one study representing Indonesia was included, with a reported prevalence of 24.0% (CI: 22.0% to 28.0%). Based on pregnancy status, pregnant women across Southeast Asia had an estimated pooled prevalence of 24.0% (CI: 17.0% to 31.0%) compared to non-pregnant women at 32.0% (CI: 25.0% to 40.0%) (Figure 4). Based on occupation, sex workers had an estimated pooled VVC prevalence of 18.0% (CI: 7% to 32.0%) compared to non-sex workers at 33.0% (CI:

20.0% to 48.0%) (Figure 5). Finally, in terms of the diagnostic methods used in each study, diagnosis of VVC via combinatorial techniques, including fungal culture, microscopy, and molecular techniques had the highest estimated prevalence of 51.0% (95% CI: 47.0% to 56.0%), followed by diagnosis via microscopy at 31.0% (95% CI: 24.0% to 39.0%), then diagnosis via both fungal culture and microscopy at 25.0% (95% CI: 16.0% to 35.0%) (Figure 6). Clinical diagnosis of VVC accompanied by molecular techniques had a prevalence of 19.0% (95% CI: 12.0% to 27.0%), followed by a combination of culture and biochemical tests at 17.0% (95% CI: 15.0% to 19.0%). Combinatorial diagnosis of VVC via culture, microscopy, and biochemical tests resulted in a prevalence of 16.0% (95% CI: 4.0% to 34.0%). The lowest estimated prevalence of VVC was found in diagnosis solely via culture at 11.0% (95% CI: 6.0% to 18.0%) and clinical diagnosis alone at 9.0% (95% CI: 1.0% to 22.0%).

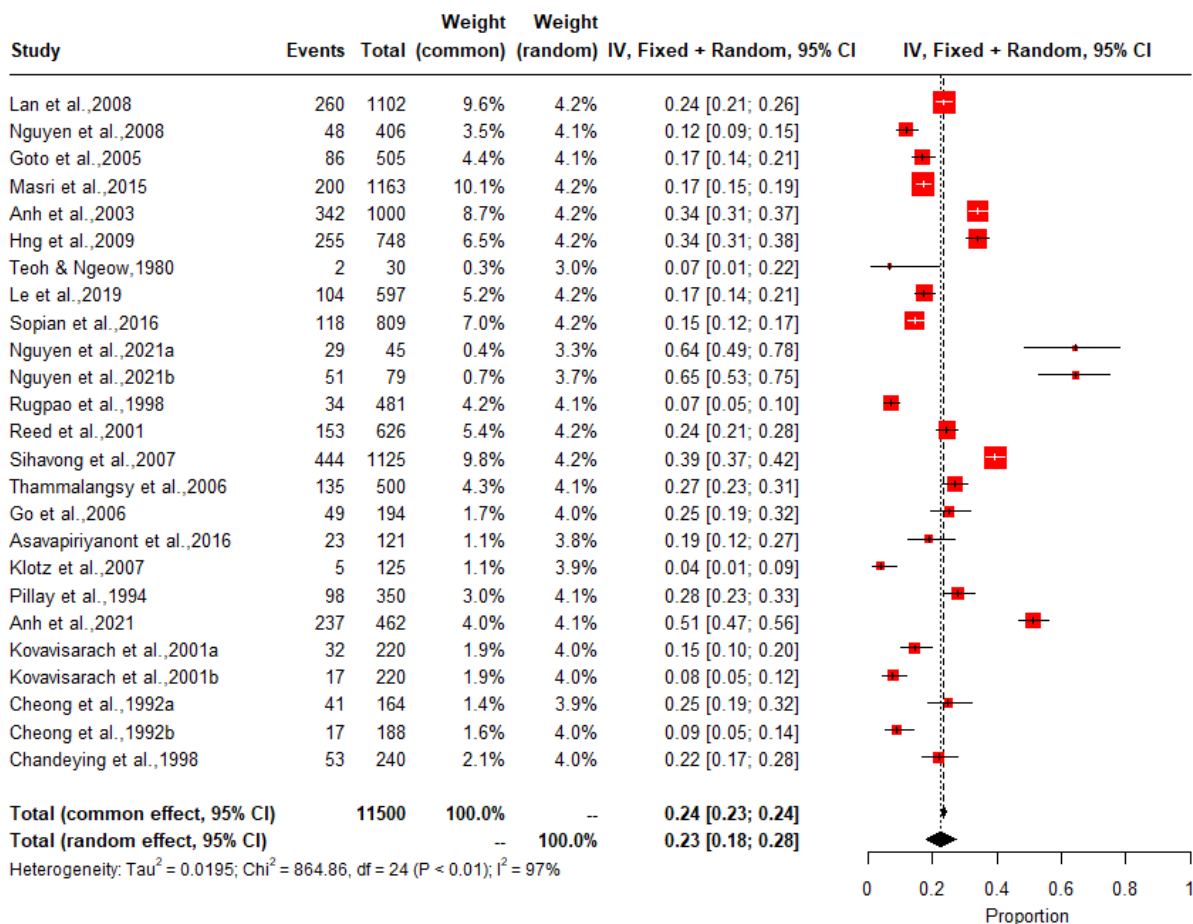


Figure 2: General prevalence of VVC among women from Southeast Asian countries.

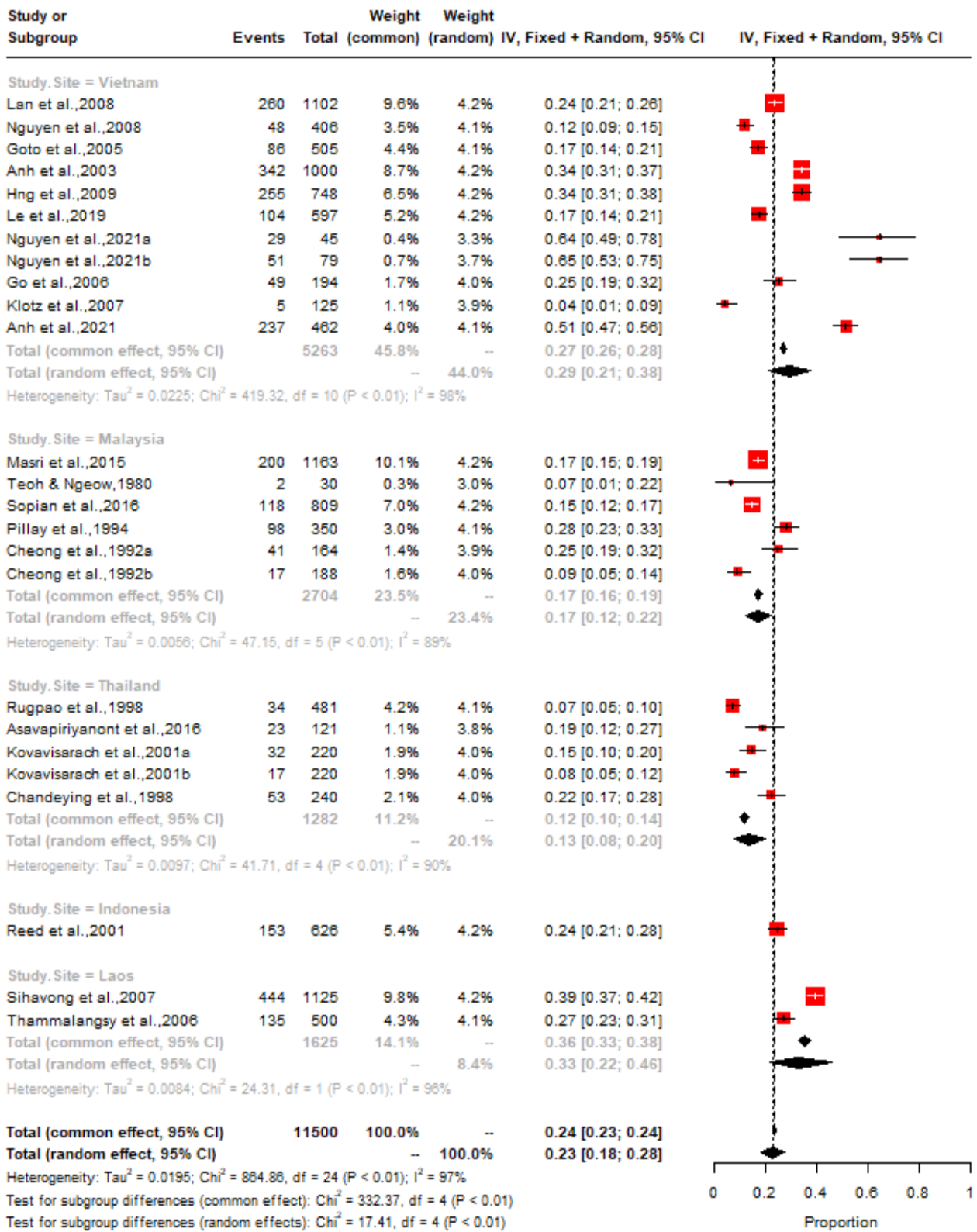


Figure 3: Subgroup analysis of prevalence of VVC across different Southeast Asian countries.

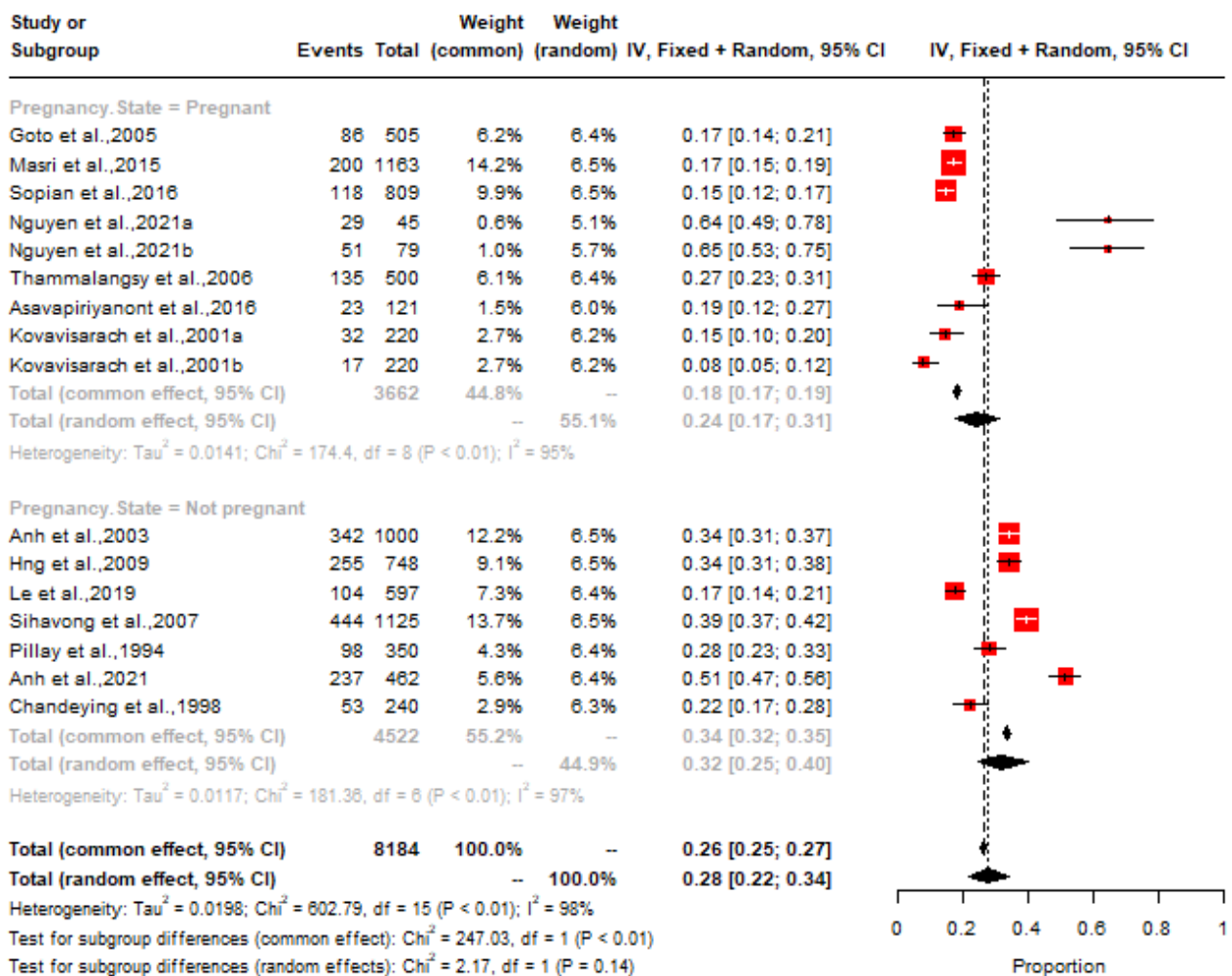


Figure 4: Subgroup analysis of prevalence of VVC among pregnant and non-pregnant women from Southeast Asian countries.

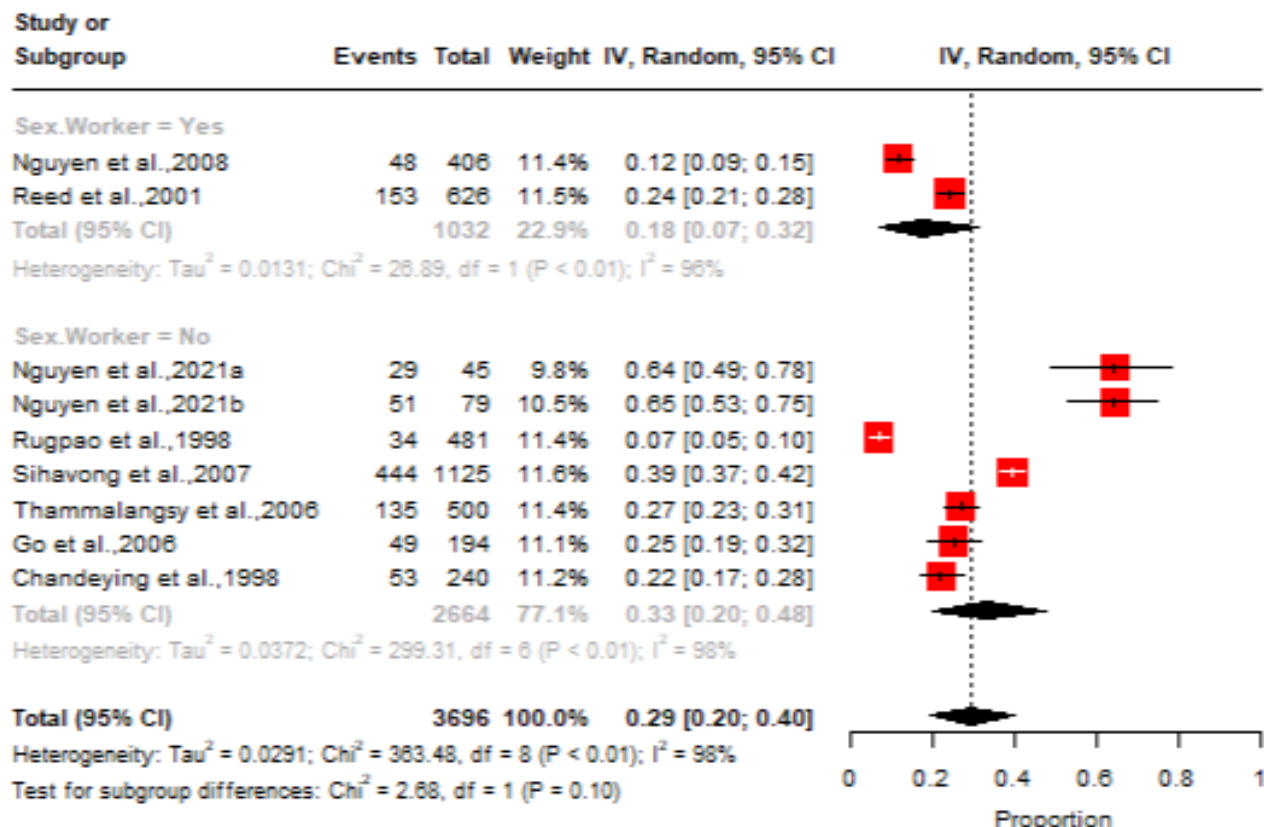


Figure 5: Subgroup analysis of prevalence of VVC among female sex workers and non-sex workers in Southeast Asian countries.

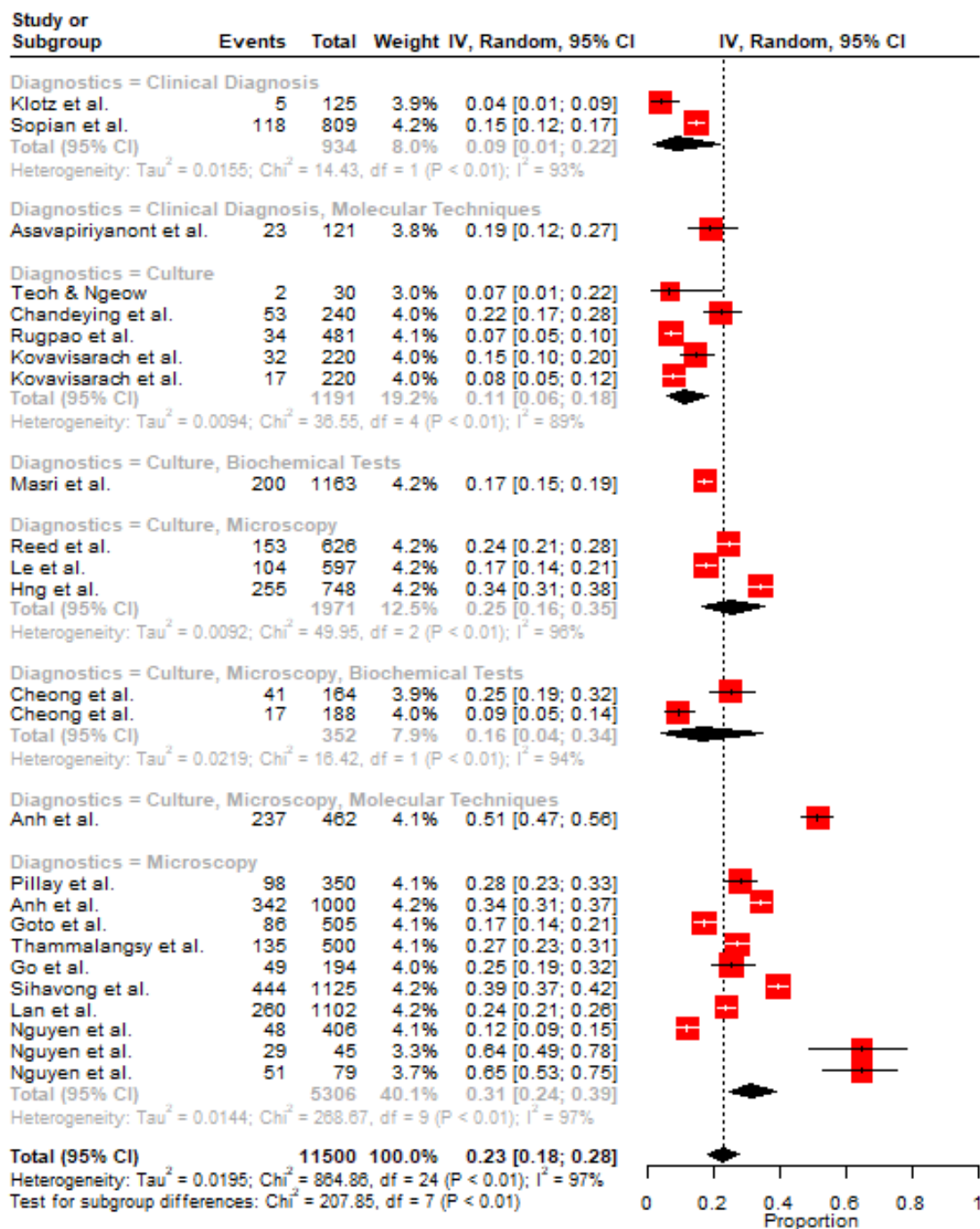


Figure 6: Subgroup analysis of prevalence of VVC based on diagnostic method used across Southeast Asian countries.

High heterogeneity exists in the pooled prevalence assessment of the studies with an I² value of 97%. Thus, the researchers grouped studies based on possible confounding factors identified; however, high heterogeneity remained despite subgroup analyses performed. Specifically, the I² values for the subgroups are the following: country analysis (97%), sex worker status (98%), pregnancy status (98%), and diagnostic methods (97%). Generally, this may be due to the temporal and geographical differences across the studies included.

DISCUSSION

The burden of VVC affects the quality of life of many Southeast Asian women. Although many studies have attempted to investigate the risk factors and burden of VVC, these have not been contextualized with women in Southeast Asia. Although the emergence of antifungal resistance across certain strains of

Candida sp. has also contributed to the growing incidence of infections across the region, studies investigating these risk factors are not conclusive and require further investigation and validation in the context of Southeast Asian countries. Thus, the study determined the prevalence of VVC across women from Southeast Asian countries and identified the disease's diagnostic tools, clinical manifestations, and risk factors using a systematic literature review and meta-analysis of various epidemiologic cohort, case-control, and cross-sectional studies. In summary, 22 articles were included for qualitative synthesis and meta-analysis of the prevalence of VVC across Southeast Asian countries. All cross-sectional, cohort, and case-control studies conducted in any Southeast Asian country were included in the current study. There is an estimated pooled VVC prevalence of 23% among women of various occupations (i.e., sex workers, non-sex workers), age groups, and pregnancy status, based on studies conducted in Vietnam, Malaysia, Thailand, Laos, and Indonesia.

Geographic Distribution of VVC across Southeast Asian Countries

The geographic distribution of VVC cases is highly variable and can be attributed to several factors, such as differences in healthcare access and contraceptive use, among others. The study by Do and Koenig reported the increased use of condoms in urban women (12%) compared to rural women (5%) in Vietnam (Do & Koenig, 2007). These practices may decrease the risk of contracting candidiasis during sexual encounters. Moreover, sociocultural behaviors across different countries on gynecological practices may vary, affecting the reporting frequency of VVC (Lan et al., 2008). The predominating perception of gynecological checkups being reserved for married women discourages unmarried women from going to gynecological clinics despite their availability. This behavioral phenomenon, in turn, encourages self-medication, leading to underreporting of VVC and unregulated antifungal use, thereby predisposing women to VVC (Kim et al., 2012; Lan et al., 2008). This may also lead to sample overrepresentation in countries where upper-class and well-educated urban patients tend to predominate in gynecological clinics (Sihavong et al., 2007; Thammalangsy et al., 2006).

Previous studies have reported an estimated global prevalence of VVC of approximately 30% to 50%. However, certain regions have reported varying estimates as a result of poorer health-seeking behaviors, inaccessible gynecological healthcare facilities, higher numbers of commercial sex workers, and lower STD prevention measures. Furthermore, the estimated I^2 value indicated high heterogeneity across studies. This implies the presence of several underlying contributing factors, such as changes to public policy, healthcare accessibility, hygiene practices, and economic development, that affect the differences in the pooled prevalence, meriting further investigation.

Laos. In the current study, the estimated prevalence of VVC infections was highest in Laos. Thammalangsy et al. attributed this to the absence of appropriate preventative measures across communities at greater risk of VVC spread (Thammalangsy et al., 2006). Despite both Thammalangsy et al., 2006 and Sihavong et al., 2007 reporting low condom use and sex work to be important factors implicated in VVC risk, sample demographics may prove to be a larger factor in the possible overestimation of VVC prevalence. Although sexual encounters between unmarried couples are not uncommon, cultural perceptions of gynecological checkups discourage many women from availing of these services (Thongmixay et al., 2020). This is aggravated by increased self-medication practices for reproductive tract infections (Sihavong et al., 2006, 2007). Studies show that upper-class and well-educated urban patients are the primary study population captured. Thus, other populations might be underrepresented (Sihavong et al., 2007; Thammalangsy et al., 2006). On the other hand, barriers to condom use, such as poverty, geographical limitations, and provider-restricted contraceptive access, were also suggested to influence increased risk for VVC and other reproductive tract infections (Thongmixay et al., 2020).

Vietnam. Recent studies have documented the growing concern posed by the emergence of azole-resistant *Candida* strains, owing to the indiscriminate prescription of antifungal drugs. As a result, reports of drug-resistant VVC infections have steadily been increasing across different parts of Vietnam (Intra et al., 2022). Moreover, the study of Lan et al. documented the widespread use of IUD contraceptives (37%) in women compared to condoms (5.4%). These government-sponsored IUDs may contribute to the predisposition of women to VVC, especially in rural areas where alternative contraceptives are less available (Gonçalves et al., 2016; White et al., 2001). Aside from reporting impeded access to contraception, vaginal douching

practices using salt water, green tea, or betel leaves in fresh water were also identified to contribute to VVC incidence by introducing changes to the vaginal microflora (Lan et al., 2008). Beyond the aforementioned factors, age must also be recognized as an important risk factor, necessitating interventions for younger women (Go et al., 2006).

Thailand. The prevalence of VVC in Thailand is poorly documented, and the absence of routine screening limits the overall accuracy of the findings of the current study. The study by Ruggao et al. attempted to investigate the risk of various gynecological conditions with HIV infection among women from Thailand (Ruggao et al., 1998). Although a positive trend was identified between VVC and decreasing CD4 count, this was not significant and requires further investigation. Nevertheless, to reduce HIV-associated complications among VVC patients, better control strategies must be implemented. Regarding the immunologic aspect of VVC susceptibility, Kovavisarath et al. investigated the aerobic microbiota of women with premature rupture of membranes. From the findings of their study, *Candida albicans*, one of the primary causative agents of VVC, was identified as the most prevalent microorganism. Therefore, these findings reinforce the increased risk of opportunistic infections due to perturbative comorbidities. In a separate study by Asavapiriyant et al. on the association of STI prevalence with teenage pregnancy, factors that were identified included the lack of routine screening due to high costs, leading to poorer health-seeking behaviors and inadequate awareness about STIs (Asavapiriyant et al., 2016a). As a result, many STIs are misdiagnosed due to the absence of symptoms. This poses a problem since the presence of comorbidities may lead to poorer pregnancy outcomes and other disease manifestations (e.g., pelvic inflammatory disease). The need to institutionalize intersectoral reforms through the implementation of routine screening for women at risk of STIs, together with proper preventive strategies for both women and their partners, would aid in reducing the overall risk and incidence of VVC (Leekuan et al., 2022; Tangcharoensathien et al., 2015). Although health-seeking behaviors are high, more proactive methods are necessary to improve the overall quality of sexual reproductive health in Thailand (Chayachinda et al., 2022).

Malaysia. Masri et al. highlighted that the widespread use of prophylactic and antifungal practices in Malaysia may have contributed to the shift in species of *Candida* causing VVC (Masri et al., 2015). These practices may explain the lower prevalence of VVC, which may, however, drive selection patterns that increase the prevalence of resistant species of *Candida*. This was evident in the study of Masri et al., which showed an increase in fluconazole-resistant species of *Candida* in Malaysia (Masri et al., 2015). The predominant infection of *Candida* sp. in Malaysia has been reportedly systemic. Since systemic infection is not routinely checked in Malaysia, this might lead to a reported lower prevalence of VVC despite increasing antifungal resistance. These patterns vary over time and across other regions, necessitating improved disease monitoring practices. In terms of the effect of comorbidities on disease susceptibility, diabetes mellitus was identified to be one factor often under scrutiny, especially among pregnant women where there is an increased risk of uncontrolled diabetes. However, Sopian et al. showed that diabetes, among other factors tested, was not directly associated with the risk of yeast infection. Inherent limitations included the multiracial nature of the population of Malaysian regions, the variable use of antibiotics, OCTs, hormonal replacement therapies, and even biological factors such as the menopausal status of women (Sopian et al., 2016). Further studies are necessary to validate the exact relationship between VVC infections and comorbid conditions.

Indonesia. Reed et al. showed that increased prevalence of VVC infection was associated with illiteracy and poor educational level, highlighting the importance of educating patients about the importance of proper hygiene and the pertinent risk factors to avoid disease, consistent with previous findings (Binsaad & Al-Abd, 2021; Reed et al., 2001). Poor health-seeking behaviors were identified as one of the most significant causes of poorer health outcomes (Arora et al., 2014). Ang et al. highlighted the importance of addressing a patient's disease-related emotional and social distress to improve overall quality of life (Ang et al., 2022). Although the estimated prevalence of VVC for regions such as Malaysia and Thailand was relatively lower, further studies are still needed to ascertain that these findings are not due to underreporting or insufficient disease surveillance. Thus, local healthcare centers and clinics must be sufficiently equipped with the tools to facilitate diagnosis and provide necessary treatments for patients (Chayachinda et al., 2021).

Furthermore, Huang et al. cited integrating clinical and laboratory findings to address and manage VVC sufficiently. Factors related to the patient's physical, emotional, and economic status must also be identified and considered to address challenges that may arise (Huang et al., 2023). This includes changes in lifestyle, improved patient awareness and health-seeking behaviors through proper education, and the establishment of proper facilities for disease management.

Other Risk Factors for VVC in Southeast Asian Countries

Overall, the impact of VVC is heavily grounded on the implications of host risk factors. In particular, risk factors such as poor disease awareness and health-seeking behaviors may lead to poorer disease outcomes. Historically, this remains a long-standing problem, especially among Southeast Asian women where cultural beliefs and stigmatization often impede women from attaining the quality of care needed and instead resort to self-medication (Feng et al., 2018; Rodgers & Zveglich, 2021; Yano et al., 2019).

Comparatively, the prevalence of VVC was estimated to be higher among non-pregnant women when compared to pregnant women. Previous studies showed that pregnant women, due to higher levels of estrogen and glycogen content in vaginal secretions, resulted in increased susceptibility to VVC infection (Soong & Einarson, 2009). Disha and Haque cited increased risk for VVC during the last trimester of pregnancy. Moreover, other factors such as a weakened immune system, altered sex hormone levels, and low vaginal pH may also contribute to VVC risk during pregnancy (Disha & Haque, 2022). Furthermore, VVC infection also shapes the vaginal microbiome, which is directly associated with pregnancy outcomes and fetal health status. In particular, a study by Dong et al. showed that infection with *C. albicans* was associated with increased abortion rate and impaired placental development among mice models, particularly modulating placental angiogenesis by downregulating several essential genes (Dong et al., 2022). However, this mechanism has yet to be fully elucidated, and several factors remain ambiguous in linking VVC with pregnancy outcomes. Therefore, further investigations are necessary to identify what may underlie the increased prevalence of VVC among non-pregnant women compared to pregnant women. Possible host-independent factors may include early diagnosis and intervention during prenatal care using available treatments (e.g., clotrimazole, miconazole nitrate, and nystatin), emphasizing the importance of regular health monitoring of pregnant women.

In the study by Reed et al., higher rates of genital infections were noted to occur among female commercial sex workers from low-priced brothels. Although perceptions of frequent genital cleansing before and after intercourse suggest reduced incidence

of infection, several disparities exist which may contribute to the overall susceptibility to disease manifestation. Firstly, introducing foreign bodies may result in alterations of host natural defenses. Secondly, genital cleansers may inhibit the growth of pathogens and disturb the natural host microflora, thereby increasing the risk of infection (Reed et al., 2001). In a study by Nguyen et al., douching practices among female sex workers were associated with reduced risk of VVC due to better patient-seeking behaviors, and awareness and differences in self-care practices.

Moreover, the increased burden of disease attributed to STIs suggests the need for better management through periodic examination and the prescription of appropriate treatments (T. V. Nguyen et al., 2008). HIV was identified as one of the most prevalent comorbid conditions for VVC (Rugpao et al., 1998). Therefore, better management strategies for HIV-associated complications among women with VVC are necessary to improve disease outcomes (Alves Teixeira et al., 2015; Boon et al., 1999; Rugpao et al., 1998).

VVC Diagnostics in Southeast Asian Countries

The diagnosis of VVC typically relies on clinical, microscopic (i.e., Gram-stain and KOH), or culture-based diagnosis (Arafa et al., 2023; Nyirjesy et al., 2022). The culture-based approach remains the gold standard for diagnosing yeast infections (Hong et al., 2013). However, in the current systematic review, microscopy (16/25) was the most utilized diagnostic tool to verify clinical diagnoses, which, in previous studies, has shown relatively poorer sensitivity (Hong et al., 2013). As a result of the nonspecific nature of symptoms and signs of VVC, solely relying on clinical findings remains the least sensitive and specific way to diagnose the disease (Hong et al., 2013; Nyirjesy et al., 2022). Due to its ease of use and reduced time needed, microscopy, in conjunction with effective clinical history taking and physical examination, remains the preferred and most widely utilized form of diagnosis for VVC among Southeast Asian countries. However, this approach may lead to misdiagnosis of the patient's symptoms or the provision of unnecessary treatment.

Findings from the current review show that a culture-based approach, in conjunction with microscopy, provides estimates of disease prevalence similar to what was estimated for the overall prevalence of VVC among Southeast Asian women. This also allows further investigation of the susceptibility profiles of organisms when planning treatment courses for patients. However, a combinatorial approach to diagnosing VVC using fungal culture, microscopy, and molecular techniques showed an increase in the estimated prevalence of VVC compared to a culture-based approach with microscopy. This finding reinforces the potential of molecular techniques in identifying patients with VVC with greater sensitivity and specificity when compared to conventional diagnostics tools. The use of such molecular methods (e.g., PCR) may provide a promising alternative for the diagnosis of yeast infections, thereby improving the overall quality of management of the disease (Asavapiryanont et al., 2016b; Hong et al., 2013; Nyirjesy et al., 2022). Currently, only two of the 25 study groups included in the current review reported the use of molecular tools in diagnosing the disease.

VVC Management and Therapeutics among Southeast Asian Women

There is an urgent need to shift the primary goal of VVC management from a disease-centric approach to one that recognizes the multifactorial etiology of the disease to improve strategies to reduce cases across Southeast Asian countries. This involves directly addressing environmental factors while considering individual risk factors such as the host immune

system, microbiota diversity, genetic background, and age (Moreira et al., 2018). Other risk factors include comorbid conditions (e.g., diabetes mellitus, other STIs) and vaginal douching, which must also be considered due to their role in shaping overall health outcomes (Arfiputri et al., 2018). Finally, the type of *Candida* sp. pathogen may also directly affect the risk of VVC infection and the design of effective therapeutic interventions due to the possibility of intrinsic species-specific phenotypic characteristics shaping the overall effectiveness of treatments (Ng et al., 2015; Parazzini et al., 2000; Yang et al., 2003). This is especially relevant to the emerging concern of drug-resistant *Candida* strains (Sustr et al., 2020). One key strategy would be improving clinic delivery services that provide antenatal, STD management, outpatient care, and family planning services. This would enable improved early detection of risk factors and disease and allow individualized treatments to be administered (Ekong Ndifreke et al., 2021).

Moreover, improved regulations on prescribing antifungals with documented cases of multidrug-resistant strains must be enforced. Currently, several species of *Candida auris* and *Candida albicans* have exhibited resistance to routinely utilized drugs (e.g., fluconazole, itraconazole, voriconazole, clotrimazole, miconazole, 5-fluorocytosine) (Huët et al., 2021; B. V. G. Nguyen et al., 2024; Tan et al., 2019). Similar resistance patterns were also found across *Candida glabrata* species against echinocandins isolated in Thailand, necessitating more careful monitoring of other types of antifungals as well (Thunyaharn et al., 2021).

CONCLUSION

The prevalence of VVC across Southeast Asian countries is 23.0% (95% CI: 18.0% to 28.0%), with variations arising from several factors, such as host-specific and geographic differences, leading to inconsistencies in the quality of healthcare delivery. Improved surveillance and regulations on antifungal use are essential to mitigate the potential risk posed by the emergence of multi-drug resistant species of *Candida* (i.e., *Candida auris*). Effective management strategies must consider the clinical presentation of VVC, typical of Southeast Asian women, as highlighted in the current systematic review, as these may vary when compared to other geographic regions globally. Overall, further investigations on the risk factors for VVC are necessary to improve diagnostics and provide a better overview of the current state of VVC distribution among Southeast Asian women.

To improve the overall applicability of the findings of the current study, further investigations must be conducted across a wider geographic scope and among women of different age groups, occupations, educational attainment, marital status, and pregnancy status. This would enable better identification of specific cohorts more susceptible to the disease. Moreover, sustainable public awareness and prevention initiatives must be established based on the specific needs that must be addressed.

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CONFLICT OF INTEREST

No potential conflict of interest was reported by the author(s).

CONTRIBUTIONS OF INDIVIDUAL AUTHORS

RGF contributed to the conceptualization, methodology, software, validation, formal analysis, investigation, data curation, writing – original draft, writing – review and editing, visualization, and project administration. RUA contributed to the conceptualization, methodology, software, validation, formal analysis, investigation, data curation, writing – original draft, writing – review and editing, and visualization. JVG contributed to formal analysis, investigation, writing – original draft, and writing – review and editing. OGT contributed to the conceptualization, methodology, software, resources, writing – review and editing, and supervision.

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