

The worldwide prevalence of anxiety in acquired immune deficiency syndrome patients: A systematic review and meta-analysis

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Abstract

Background: Anxiety affects social, economic, and physical aspects of daily life in patients with AIDS. Therefore, it is necessary to take preventive measures and design plans to maintain their general health. The present study was the first comprehensive systematic literature review research that examined the worldwide prevalence rate of anxiety in patients with AIDS.

Methods: We searched for papers published in the English language in the major databases including Embase, PubMed, Web of Science, Scopus, Cochrane, and Google Scholar from 2000 to October 2018. There were 40 studies which found to be eligible. These studies were independently evaluated and the collected data were entered in a data extraction form, which was then analyzed by two authors and a third author if necessary. Der Simonian-Laird model was used to estimate the prevalence rate on a Forest plot at the interval confidence of 95%.

Results: The total sample size was 24111, and the total number of people with anxiety was 5546. The results based on the random-effects model showed that the rate of anxiety prevalence in the patients was 25% (CI: 95%, 21% -30%) with heterogeneity of 97.9% and a significance level of $p < 0.001$. The South America continent with a prevalence of 38% (95% CI, 34%-42%) had the highest anxiety prevalence rates and Africa with 19% (95% CI, 12% -29%) had the lowest anxiety prevalence rates.

Conclusion: Based on findings, the prevalence of anxiety in developed countries was partially higher than in underdeveloped countries and the obtained mean in the present study. It can be a significant point for policymakers. Therefore, WHO and the world community should have special plans for these countries.

Keywords: Worldwide, Prevalence, Anxiety, Acquired Immune Deficiency Syndrome, HIV

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↑What is “already known” in this topic:

Some studies have shown that a significant percentage of patients with HIV suffer from mental disorders, including stress and depression, and most importantly anxiety, which can double the burden of the disease and reduce the quality of life in these individuals.

→What this article adds:

The results based on the random-effects model showed that the rate of anxiety prevalence in the patients was 25% (CI: 95%, 21% -30%). The results also showed that anxiety was more prevalent in men (6%) than women, but there was no significant relationship between gender and anxiety rate.

Introduction

The international community is currently facing the spread of infectious diseases such as AIDS and hepatitis, which are serious threats to public health. The epidemic of these diseases has imposed a burden on human societies and health systems of countries with the major challenges of controlling, confronting and treating such diseases (1). In addition to endangering public health, these diseases have several economical, social and cultural impacts. They are also mentally demanding for the infected patients and often cause mental disorders such as anxiety and depression (2). It is said that more than 6,800 people are infected with HIV every day, and more than 5,700 people die of AIDS (3). According to a report published by the World Health Organization (WHO), 36.9 million people were infected with HIV by the end of 2017.

Some studies have shown that a significant percentage of patients with HIV suffer from mental disorders, including stress and depression, and most importantly, anxiety, which can double the burden of the disease and reduce the quality of life in these individuals (4). Moreover, AIDS-induced anxiety affects their performance in social relationships and daily life, which is the main reason for the exclusion they face (5). In some severe cases, these issues may lead to irreparable damages such as suicide. More importantly, anxiety in patients with AIDS may cause non-adherence to treatment, which may prolong the treatment process, and subsequently increase the costs for the patients and their families and impose an additional cost on the health system and individuals (6).

According to recent studies, the prevalence of anxiety among people with HIV was 70.25% (in 378 samples) in developed countries such as America in 2018 (7). In developing countries like Mexico and Brazil, the prevalence rates were 30.32% (in 291 cases) (8) and 70.44% (in 47 samples) (9), respectively, in 2017. The rate was 40.27% (in 4103 samples) in China in 2018 (10) while it was 40.32% (in 417 samples) in underdeveloped countries such as Ethiopia in 2016 (11).

Other studies, such as the study conducted by Betancur et al. in 2017 on the quality of life, anxiety and depression of a population infected with HIV in Brazil, have shown a rate of 7.44% indicating a moderate to high prevalence of anxiety (8). Caballero-Suarez et al. reported that the prevalence of anxiety was higher in women with HIV than in infected men in Mexico in 2017 (6). Since anxiety in AIDS patients affects the social, economic, physical and general health of the community, it is necessary to develop specific and comprehensive measures and plan for pre-

venting the complications of the disease and maintaining the health of these people. This requires accurate, integrated and categorical statistical information on the global prevalence of the disease and its related and predisposing factors (11, 12). This can contribute to healthcare systems and policymakers controlling the anxiety in the early stages of AIDS, and lead to a significant reduction in the healthcare cost for these patients. In addition, determining the exact burden of this disorder in HIV patients on the basis of the continents and countries can lead to the development of regional policies for allocating resources to areas with higher demands worldwide (13, 14).

Although there are several studies worldwide, most of them have merely focused on a few variables or have been performed at national or regional levels. The present study is the first comprehensive Systematic Literature Review (SLR) study to investigate the anxiety prevalence in HIV patients at a comprehensive and integrated level, including different aspects in the world through a systematic review and meta-analysis.

Methods

The current research was registered in PROSPERO at the University of York with registration code of PROSPERO 2019 CRD42019118955 Available from: http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42019118955 The University of York.

Search strategy

We searched English databases of PsycINFO, Embase, Web of Science, Scopus and PubMed, using MeSH standardization and the keywords including "Anxiety", "Hypervigilance", "Nervousness", "Human Immunodeficiency Virus", "Human T-Cell Lymphotropic Virus Type III", "Human T-Cell Leukemia Virus Type III", "Lymphadenopathy-Associated Virus", "AIDS Virus", "AIDS Viruses", "Acquired Immune Deficiency Syndrome Virus" from January 2000 to October 2018. This initial search resulted in 939 articles. The search started with the articles published in the year 2000 because the globally increasing prevalence of anxiety in HIV/AIDS patients was very high at the beginning of the current century. After importing the articles found into the EndNote software, the duplicates were deleted (Table 1).

Study selection

Figure 1 shows the process of the search strategy. Initially, two independent reviewers studied the titles and

Table 1. Search strategy in different databases

Database	Search Strategy
PubMed	((("Anxiety*" [TITLE-ABSTR-KEY]) AND ("AIDS*" [TITLE-ABSTR-KEY]))
Web of Science	TS= ("Anxiety*") AND TS= ("AIDS*")
Embase	'Anxiety*':ab,ti AND 'AIDS*':ab,ti
Scopus	TITLE-ABS-KEY (Anxiety*) AND TITLE-ABS-KEY (AIDS*)
PsycINFO	(Anxiety*)AND (AIDS*)
Google Scholar	"Anxiety*" AND "AIDS*" anywhere in papers

* All the keyword have been searched based on MeSH standardization

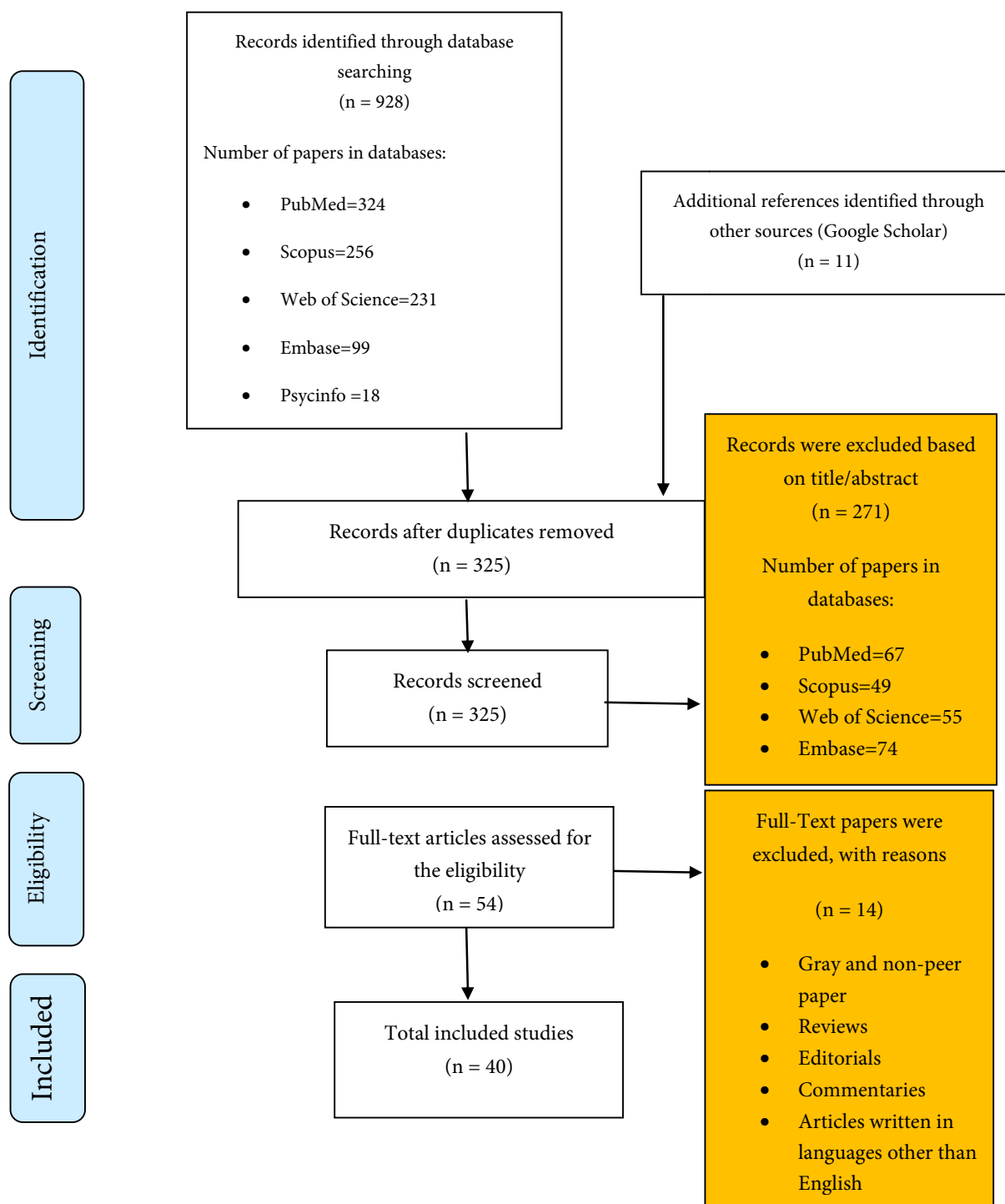


Fig. 1. Flow diagram of our review process (PRISMA)

abstracts of the articles to screen irrelevant ones based on the inclusion and exclusion criteria, thereby resulting in 54 potentially relevant articles. Then, we reviewed the full-text of articles to detect the eligible ones, which resulted in 40 articles.

Inclusion criteria

The articles were included if they were in English language, published between January 2000 and October 2018, with original research status, had full-text available,

had observational designs including cross-sectional, cohort, case-control, descriptive and prospective designs, and reporting anxiety intensity among patients with HIV/AIDS, and the prevalence rate on the basis of a set of data.

Exclusion criteria

The articles in languages other than English, published before January 2000, having designs of review, letters to editors, editorials, commentaries, expert opinions, case

studies, case-series, books, book chapters, brief reports, RCTs, and thesis, addressing therapy, follow-up, drug, and clinical decision-making, and reporting invalid figures or tables, or having difficulty calculating the prevalence were excluded.

Quality assessment of the searched articles

The quality of the articles was evaluated by using Newcastle-Ottawa Scale (NOS) for assessing observational studies. In order to reduce bias, the quality of the articles was assessed by two independent evaluators; in the case of any disagreement between the two evaluators, the article was discussed in the presence of a third evaluator to reach the consensus. The NOS is used to select the articles suggested by the Cochrane Collaboration. It allocates a maximum of 9 points for the minimum risk of bias in the three areas in cohort and case-control studies and systematic reviews. This scoring includes four points for selection of study groups, two points for comparability of groups and three points for ascertainment of exposure and outcomes. Three or 4 points in the selection area, 1 or 2 stars in the comparability area, and 2 or 3 stars in the outcome/exposure area indicate that the article has a good quality. Two points in the selection area, 1 or 2 points in the comparability area, and 2 or 3 points in the outcome/exposure area suggest that the article has a fair quality. Zero or 1 point in selection area, 0 point in comparability area, and 0 or 1 point in outcome/exposure area show that the article has poor quality (15).

Extraction of required data

As shown in Appendix Table 1, the required data consist of general information (name of the author, year of publication, name of the journal, name of the publisher, type of study, and quality of study) and specific information (sample size, prevalence of anxiety, number of male/female participants, country, continent, regional classification of WHO, educational level, marital status and type of questionnaire used).

Statistical analysis

Der Simonian-Laird model was used to estimate the prevalence rate on a Forest plot at the interval confidence of 95%. The heterogeneity (I^2) and meta-regression analysis were computed on the basis of the publication year and sample size. The stability result was confirmed by sensitivity analysis. Subgroup analysis was performed by using the collected data, including sample size, place of study, year of publication, gender, type of study, and quality of study. The publication year and sample size were utilized to perform the cumulative meta-analysis. The Egger test was applied for publication bias and Comprehensive Meta-Analysis software of data analysis.

Results

Search results

The results of the current study, based on the PRISMA protocols, are shown in Figure 1. The initial search of five different databases resulted in 928 articles from which the duplicates were removed and 325 articles remained. After

reviewing the abstracts and full text of the articles, 271 articles were removed, and 54 articles with available full texts fulfilled the eligibility criteria. However, 14 articles were also removed for some other reasons. Finally, on the basis of the inclusion and exclusion criteria, 40 articles were selected for final review (Fig. 1). The selected studies were published between 2000 and October 2018. The total number of patients participating in these studies was 24,111 (Appendix Table 1).

Distribution of articles by the year of publication

Figure 2 shows the process of publishing articles on anxiety in patients with AIDS from 2000 to October 2018. The findings reveal that no article was published on this topic before 2002, and the number of published articles did not exceed two from 2002 to 2011. As seen in Figure 2, there has been a significant increase from 2012 onwards to the highest level (10 articles) in 2018 (Fig. 2).

Overview of the prevalence of anxiety

After entering the main data of the 40 selected studies in an Excel form and initial analysis of the data, the total number of patients with anxiety was found to be 5546 out of the total samples taken in these studies ($n=24111$). The results of the analysis based on the random-effects model indicated that the global prevalence rate of anxiety in these patients was 25% (95% CI=21% -30%) with a heterogeneity of 97.9% and a significance level of $p<0.000$ (Fig. 3).

The prevalence of anxiety based on the continents

As it is seen in Appendix Figure 1, for depicting the prevalence of anxiety based on the continents, each continent is shown by a specific color. Countries with darker colors in each continent represent a higher prevalence rate of anxiety in patients with AIDS in that area compared with other parts of the same continent. The black spots on the basis of different sizes show the number of studies in each continent. According to the findings, the anxiety prevalence rates in the continents, except for Africa, are somewhat similar to each other, with the highest prevalence of 38% (95% CI= 34% -42%) in South America, where the anxiety is noticeable in the patients mostly in the northern region of the continent, namely the Brazilian state. On the other hand, the findings show that Africa has the lowest rates of anxiety, 19% (95% CI, 29% -12%), with the highest anxiety rate in South African (South Africa) and Nigerian regions (Appendix Fig. 1).

The prevalence of anxiety based on Regional classification of WHO

Employing the six regional classifications of WHO, we found that the prevalence rate of anxiety in patients with AIDS was the highest in the South East Asia region with the prevalence of 31% (95% CI=67% -10%), while the lowest prevalence rate was in Africa, 18% (95% CI=12% -29%). Interestingly, we found no study in the Eastern Mediterranean Regional Office (EMRO) region regarding this issue over the period mentioned (Appendix Fig. 2).

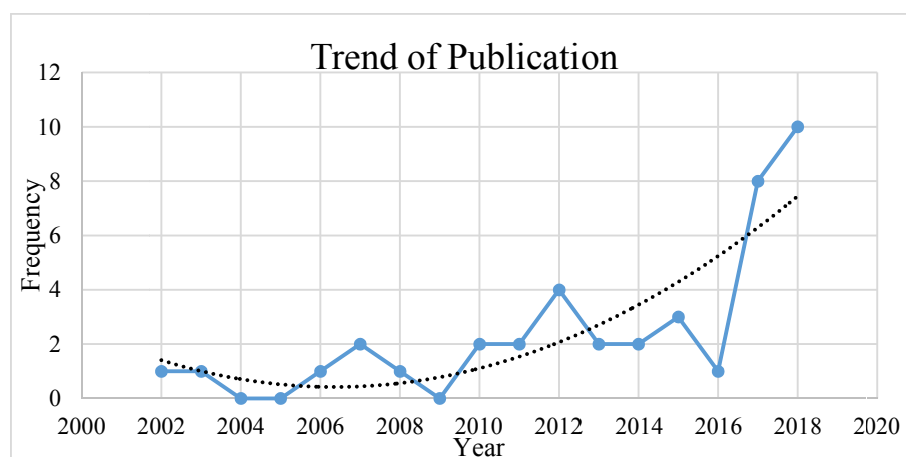


Fig. 2. Distribution of articles frequency by publication year

prevalence(Anxiety in HIV)

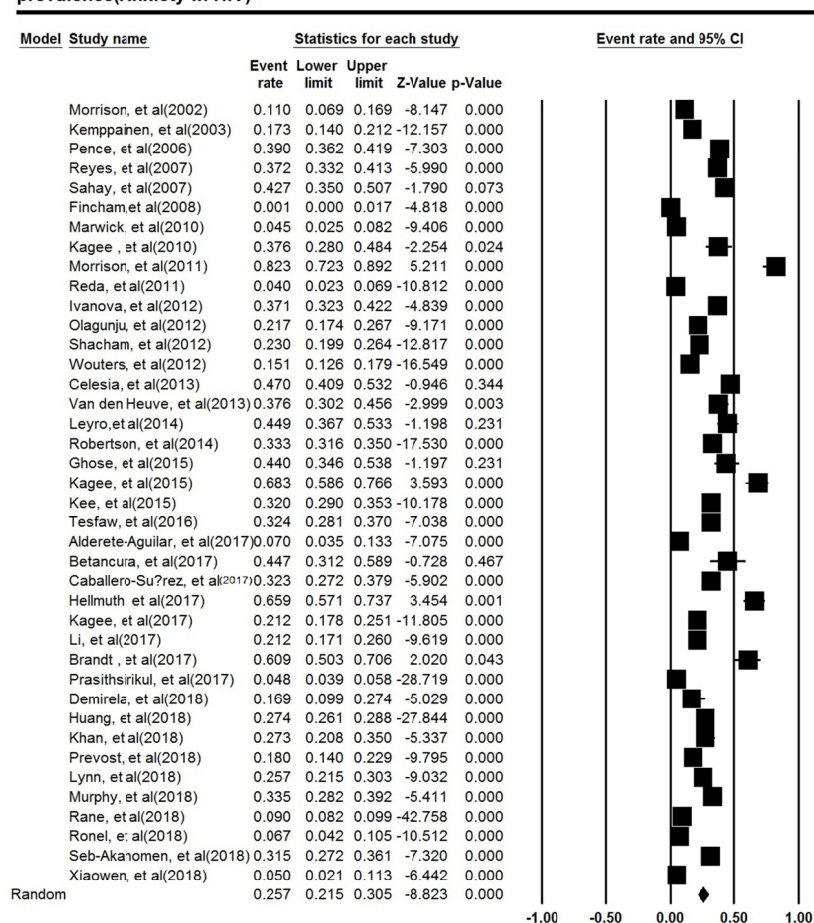


Fig. 3. Forest Plot of Worldwide Prevalence of Anxiety in HIV/AIDS patients

Other Sub-group analysis

As seen in Table 2, 17 out of 40 studies have used the HADS questionnaire, indicating that this is one of the

most commonly used questionnaires in this area. The results of the analysis revealed that the mean anxiety prevalence in the patients assessed by this questionnaire was

Table 2. The global prevalence of anxiety in HIV/AIDS patients base on the questionnaire, type of study and quality of study

Subgroups		Number Studies	Effect size and 95% interval			Test of null (2-Tail)		Heterogeneity			
			Point estimate	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared
Questionnaire	ASI-3	1	0.449	0.367	0.533						
	BAI	8	0.352	0.277	0.434	-3.449	0.001	93.36	7	<0.001	92.50
	DASS_21	1	0.273	0.208	0.350						
	GAD	5	0.216	0.121	0.355	-3.661	<0.001	239.45	4	<0.001	98.33
	HADS	17	0.192	0.143	0.254	-7.904	<0.001	794.78	16	<0.001	97.99
	HARS	1	0.110	0.069	0.169						
	ICD-10	2	0.105	0.021	0.397	-2.434	0.015	24.88	1	<0.001	95.98
	IDAS	1	0.609	0.503	0.706						
	SAS	1	0.470	0.409	0.532						
	Unknown	3	0.503	0.335	0.671	0.035	0.972	54.88	2	<0.001	96.36
Type of study	Cohort	9	0.168	0.100	0.269	-5.217	<0.001	471.23	8	<0.001	98.30
	Cross-sectional	31	0.292	0.248	0.340	-7.782	<0.001	966.43	30	<0.001	96.90
Quality of study	High	23	0.206	0.157	0.265	-7.976	<0.001	1405.31	22	<0.001	98.43
	Low	6	0.298	0.188	0.437	-2.774	0.006	97.05	5	<0.001	94.85
	Medium	11	0.359	0.295	0.430	-3.835	<0.001	165.39	10	<0.001	93.95

19% (95% CI=25% -14%). The three questionnaires, shown by the word "Unknown" in the table, were researcher-made questionnaires that were unrelated to any credible organizations and institutions. The findings in Table 1 show that 31 out of the 40 included studies have cross-sectional designs and 9 have Cohort designs, with prevalence rates of 29% (95% CI=34% -24%) and 16% (95% CI=10% -26%), respectively. Other findings based on the quality of the studies showed that 23 studies were of high quality, with a mean prevalence rate of 20% (95% CI=15% -26%) (Table 2).

The global prevalence of anxiety based on gender

The analysis showed that anxiety was more prevalent in men (0.68) than women, but there was no significant relationship between sex and anxiety prevalence rates (Fig. 4).

Meta-regressions based on sample size and the year

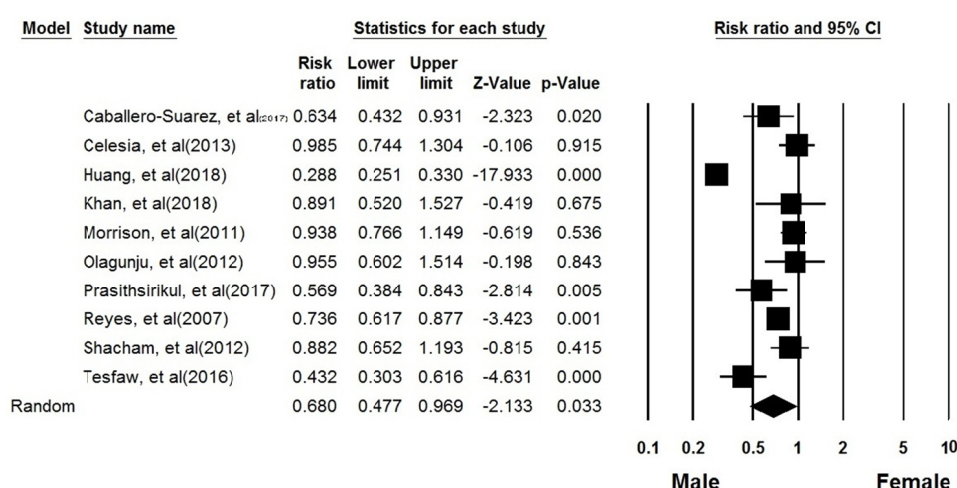
Figure 5 shows that the sample size has no effect on the prevalence rate, and 12 per 100000 people are added to the patients with anxiety.

In Figure 6, the findings indicate that there is a significant relationship between the year ($p<0.001$) and the prevalence rate of anxiety; in other words, the rate is down-trend and has about a 5% reduction per year (Fig. 6).

Publication bias

Figure 7 displays the analyses performed to detect the publication bias on the Funnel plot shows that there is no publication bias, and Egger test findings are reported to be less than 1 ($p=0.927$).

Risk Ratio of Anxiety in HIV(Male/Female)

**Fig. 4.** The Risk Ratio of Anxiety in HIV/AIDS patient base on gender

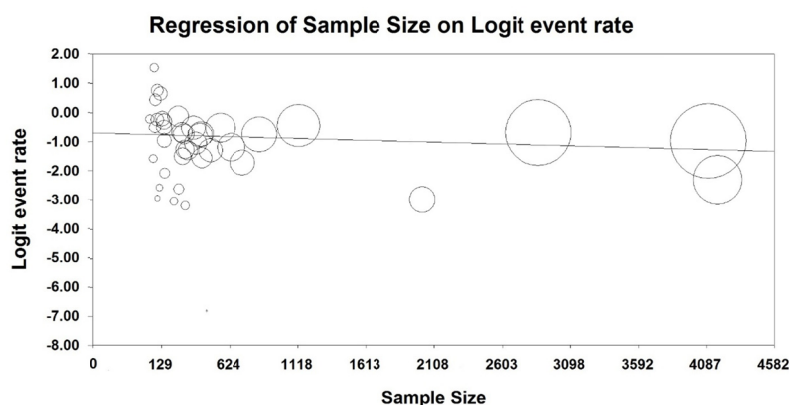


Fig. 5. Meta-regressions based on sample size

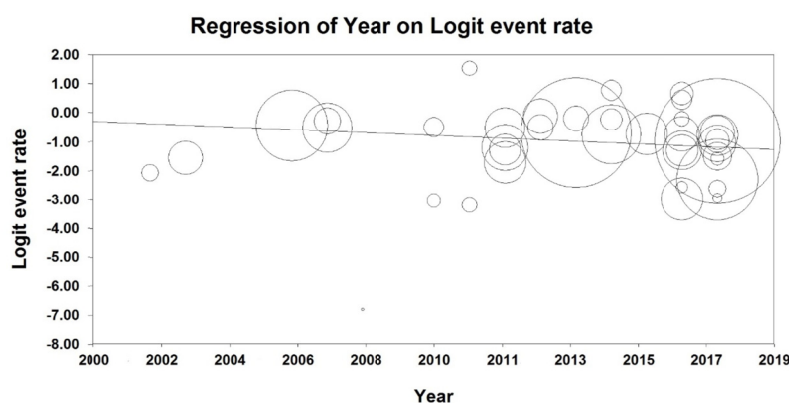


Fig. 6. Meta-regressions based on the year

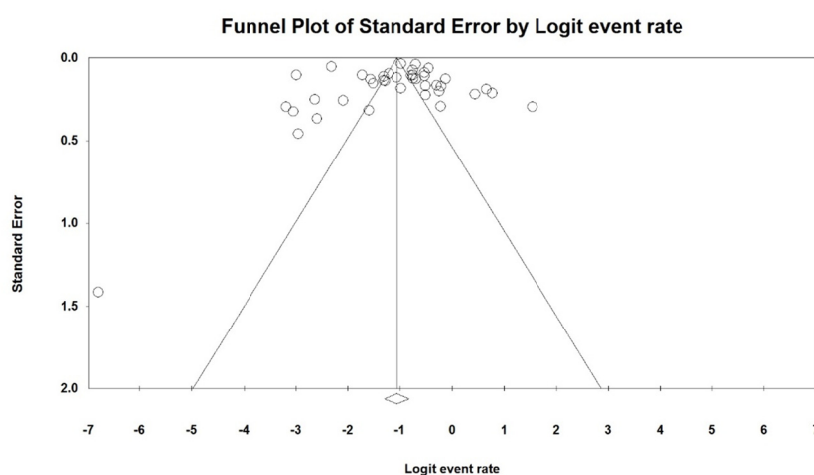


Fig. 7. Funnel plot to assess publication bias

Discussion

This is the first systematic review and meta-analysis examining the global prevalence of anxiety in AIDS patients. According to the results of this study, there is an anxiety rate of 25% in these patients. The findings of the present study suggest that the mean prevalence of anxiety

in patients with AIDS in developed countries is higher than the mean obtained in our study. According to the findings of one of the studies, 45% of 136 AIDS patients suffer from anxiety in the United States (16). Another study on 1125 people has reported that the anxiety prevalence rate is 39% (17). On the other hand, several studies

have reported that the prevalence rates are 47% and 34%, in the studies related to Italy and the UK, on 251 and 278 people, respectively (18, 19). In the studies of less developed countries, the results indicate that the prevalence rate is less than the mean of 25% of the present study. For example, a study in South Africa on 4170 patients with AIDS has reported that the prevalence rate is 9% (3). Additionally, an anxiety prevalence rate of 5% has been found in a study on 2023 patients with AIDS in Thailand (11).

The results of the present study indicate that there is a significant correlation between sex and anxiety ($p < 0.001$), and the prevalence of depression in men with AIDS is higher than that of women. Similarly, in a study conducted on 557 patients with AIDS in Puerto Rico, the anxiety prevalence rate in the men was reported to be more than in the women ($p < 0.01$) (20). In contrast, a study performed by Caballero-Suárez et al. on 291 AIDS patients in 2017 suggests that there is a significant relationship between gender and anxiety, but women are more susceptible to anxiety than men (7). However, two studies carried out in Albania and Nigeria have shown that there is no significant relationship between sex and anxiety in patients with AIDS (21, 22).

Although there are some studies indicating that there is no significant relationship between the educational level and prevalence rate of anxiety in people with AIDS (16, 23), Huang et al. examining 4103 AIDS patients, has shown that the prevalence rate is more common in people with higher educational level which could lead to the awareness of educated people about the future and the consequences of the disease (9).

Another variable, usually associated with a significant correlation with anxiety and depression among individuals, is the marital status (24). Seb-Akahome et al. have remarked that single females, especially divorced women, have a higher risk of anxiety, whereas another study in Nigeria has reported that there is no significant relationship between marital status and anxiety in these patients (25).

Conclusion

The present systematic review and meta-analysis examined the global prevalence of anxiety in patients with AIDS. It is the first study examining anxiety from different aspects. Based on the findings, the mean prevalence rate of anxiety in patients with AIDS in some developed countries, which was slightly higher than that of the underdeveloped countries, appeared to be higher than the mean obtained in the present study. This is a major finding which should be taken into consideration by policy-makers in this area because the special conditions of patients with AIDS and their relatives may cause anxiety with adverse consequences such as non-adherence to treatment, prolonged treatment, social rejection, additional costs added to the treatment costs. The findings of this study can contribute to the promotion of evidence-based decision-making for planning and providing better healthcare services for this group of patients.

Limitation

The main constraints of this study were the lack of information about some countries, making the likelihood of inaccurate reports of the incidence of anxiety in patients with AIDS in those regions and continents. This could be a suggestion for future studies and research. On the other hand, the results of the present study have a high level of heterogeneity; most studies were cross-sectional, and some of them used convenience sampling, while some others applied cluster sampling methods. Consequently, caution should be taken in applying the findings to future policies and plans.

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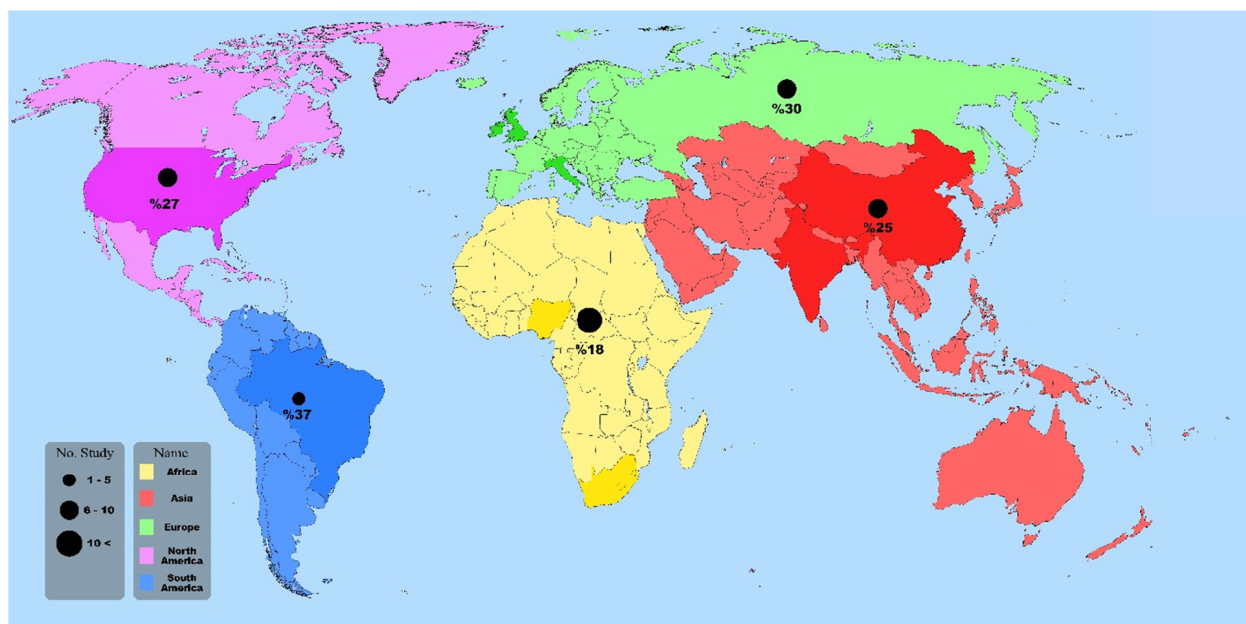
Conflict of Interests

The authors declare that they have no competing interests.

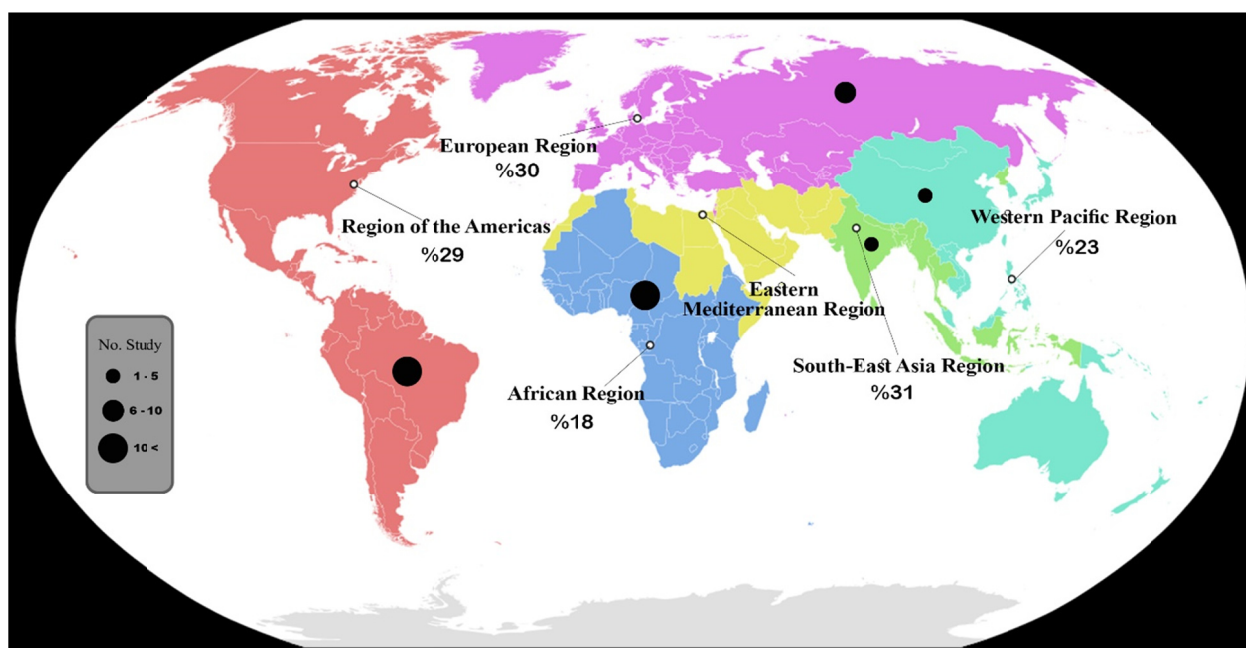
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Appendix Fig. 1. Number of studies & the global prevalence of anxiety in HIV/AIDS patients based on Continents, 2000-2018. (Size of dots indicates the number of studies and the colors show the continents. Map created with PhotoshopCC, using WHO criteria for political borders.



Appendix Fig. 2. The global prevalence of anxiety in HIV/AIDS patients based on WHO Regions & Number of studies, 2000-2018. (Size of dots indicates number of studies and the colors show the continents. Map created with PhotoshopCC, using WHO criteria for political borders.