Burden of cervical lesion in Ethiopia: Systematic review and meta-analysis

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Abstract

Though cervical cancer is largely preventable, it is still the second most common female cancer globally and the leading cause of cancer deaths among females in African. Though many efforts has been done to study the burden of the disease in Ethiopia, there are still fragmented primary studies reported cervical lesion. Hence, this systematic review and meta-analysis aimed in estimating the pooled prevalence of cervical cancer and its trend in Ethiopia. Methods: This systematic review and meta-analysis was conducted using available data. PubMed, Web of Science, SCOPUS, Science Direct, Google Scholar, African Index Medicus (AIM), African Journals Online databases and Ethiopian University research repositories were searched following the Preferred Items for Systematic review and Meta-analysis (PRISMA) guideline. STATA 15 statistical software was used to analyse the data. The quality of included studies was assessed using the Joanna Briggs Institute (JBI) quality appraisal tool for meta-analysis. Heterogeneity between studies was assessed using Cochrane Q test and I2 test statistics based on the random effects model. A random effect model was computed to estimate the pooled prevalence of cervical lesion in Ethiopia. In addition, the trend of cervical lesion in the country was depicted. Result: Fifteen studies with a total of 25,348 participants were included in the analysis. The overall pooled prevalence of cervical lesion was 16.36 (95 CI: 10.97-21.75). The subgroup analysis by region showed the highest prevalence of cervical lesion at the Southern Nations and Nationalities Peoples Region (19.65%; 95% CI: 15.51 – 23.80). The trend of cervical lesion showed an increased pattern overtime from 1992 to 2018 in the meta-regression analysis. Conclusion: One among six of the study participants had cervical lesion. The trend also showed that there is still an increased cervical lesion in the country. Best practices in achieving high vaccination coverage shall be adapted from other successful countries. Key words: Cervical cancer, cervical lesion, systematic review, Ethiopia

Background

Cancer is a group of more than 100 different diseases that can be characterized by its uncontrolled cellular growth, local tissue invasion, and distant metastases (1,2). Most patients and their families don't properly know what a cancer is and its treatment options. Consequently, 80% to 90% of cancer patients already suffer from advanced and incurable cancers at the time of diagnosis (3–5).

Cancers that originate in the female reproductive system are called women's reproductive cancers. These include cancer of the cervix, breast, ovaries, vagina, vulva, and endometrium (3,6,7). Though cervical cancer (CC) is largely preventable, it is still the second most common female cancer internationally and the leading cause of cancer deaths among females in African (8,9).

Low level of awareness, lack of effective screening programs, overshadowed by other health communicable health priorities are the possible factors for the observed higher incidence rate of cervical cancer in the developing regions of the world (3,10).

Human papillomavirus (HPV) is a virus transmitted through sexual contact known to cause CC (11,12). Often times, HPV causes precancerous cervical lesion and cancer in women but it can be screened and treated easily before it will turn into invasive cancer (13,14).

Cervical cancer prevention and control approach is made up of several key components (15). Awareness creation, vaccine provision, accessible screening service and provision of affordable treatment facilities are among the top key approaches in the prevention and control of cervical cancer. Currently, there are two types of HPV vaccines: the bivalent vaccine and the quadrivalent vaccine, which protects against genotypes 6, 11, 16 and 18. Those two vaccines have been evaluated in large clinical trials and proven to prevent the two most important high-risk HPV types—genotypes 16 and 18—which are known to cause up to 70% of cervical cancers (16).

Concerning to screening, there are three types of cervical cancer tests. These are: 1. Cytology: conventional (Pap smear) and liquid-based; 2. HPV DNA test; 3. Visual inspection: with acetic acid (VIA) or Lugol’s iodine (VILI) (17).

Cryotherapy is a procedure that is used to remove abnormal cervical tissue from the cervix and promotes the growth of new healthy cells on the cervix. It does not require hospitalization, anesthesia, or premedication and can be completed in less than

30 minutes and does not have a long-term impact on women's fertility or pregnancy outcomes (18,19).

Of 86% of all CC diagnosed, 88% of death occur in developing regions of the world (20). Every year, 500,000 new cases are diagnosed and 270,000 women die of this disease, mostly 85% in developing countries (21,22). Cervical cancer is the second most frequently diagnosed cancer and the leading cause of cancer death in African women (23,24).

An estimated 570,000 new cases of CC was recorded in 2018. Approximately 90% of deaths occurred in low and middle-income countries(25). Rates vary substantially across regions, with the incidence and death rates in East Africa and West Africa as high as the rates in North Africa (26) .

Reports of trends in CC mortality from less developed countries have been limited by poor data quality and inaccurate population estimates (27). But because of poor access to quality screening and treatment service, the trend is increasing in these countries. According to trend analysis on CC between the year 1980 and 2010 was increased from 378 000 to 454 000 (28). By 2020, it has been estimated that CC will be diagnosed in over 665,035 women worldwide, and 357,852 will die as a result (22).

In Africa, which has a population of 267.9 million women aged 15 years and older at risk of developing cervical cancer, approximately 80,000 women are diagnosed with cervical cancer per year, and just more than 60,000 women die from the disease (29). The incidence and mortality in sub-Saharan Africa are among the highest in the world and accounts for over 70% of the global CC burden with 70,000 new cases annually (22,30).

According to the 2009 World Health Organization (WHO) report, the age-adjusted incidence rate of cervical cancer in Ethiopia was 35.9 per 100,000 patients with 7619 annual number of new cases and 6081 deaths every year (7,31–33). Records also showed that, of the nearly 22 million Ethiopian women over the age of 15, approximately 7,600 are diagnosed with cervical cancer and roughly 6,000 women die of the disease each year (31,34–36).

Though many efforts has been done to study the burden of cervical lesion, still there are fragmented primary studies reported the outcome of interest. Different previous studies and literatures showed variations in the past and across different geographical areas in the country, Ethiopia. Hence, this systematic review and meta-analysis aimed in estimating the pooled prevalence of cervical cancer and its trend in Ethiopia. In addition, the finding will provide an insight to decision and policy makers on how to strengthen the existing CC prevention and control strategies. Or device a new way of disease prevention and control mechanisms.

Methods

Reporting

The Preferred Reporting Items of Systematic Reviews and Meta-Analysis (PRISMA) checklist guideline was used to report the result of this systematic review and meta-analyses. In addition, PRISMA Flow chart was utilized to show the selection process of studies for a systematic review and meta-analysis (37).

Searching strategies

This systematic review and meta-analysis was conducted to estimate the pooled prevalence of cervical cancer and its' trend in Ethiopia. To conduct this study, all potentially relevant articles, grey literatures, and government reports were meticulously searched. We searched PubMed, Web of Science, SCOPUS, Science Direct, Google Scholar, African Index Medicus (AIM) and African Journals Online databases for all available studies using the following search terms: "Cervical cancer", "Cervix neoplasm", "Cervix lesion", "Pap Smear Positive", "Cervix precancerous lesion" and "Ethiopia". Search string was developed using "AND" and "OR" Boolean operators. In addition to this, grey literatures were searched from research repository online library and a secondary search technique known as "footnote chasing" was utilized to identify additional articles from the included articles.

The search was carried out from August 28 to October 10, 2019 and all articles published until October 10, 2019 were included in the review.

Inclusion and exclusion criteria

This systematic review and meta-analysis encompassed studies conducted only in Ethiopia using English language published from 1992 to 2018. Research articles that reported the prevalence of cervical cancer, published in the scientific journals, grey literatures were included in the review. Studies focused on the assessment of knowledge, attitude, and practice towards CC without the outcome of interest of this study, program evaluation studies, studies with only abstracts, case studies, qualitative studies and citations without full-text were excluded.

Operational definition

Cervical lesions: Lesions that are visible and defined, after the application of visual inspection with acetic acid (VIA)/visual inspection with Lugol's iodine (VILI) (38). They have borders and degrees of acetowhitening, vessel patterns, and margins. Precancerous areas are not "dark red and puffy" as the caption suggests (39).

Data extraction

Three authors (AS, TD and YB) independently searched the studies and extracted all necessary data using a standardized data extraction format using Microsoft Excel. The extracted parameters were: primary author, publication year, region where the study was conducted, method of assessment, study design, age range of the study participants, mean age of the study participants, response rate, sample size, prevalence of cervical cancer, and quality of each study. Then, four authors (GD, AE and YW) checked the data extraction process. Finally, authors (BZ, EA and WA) participated in approving and resolving the disagreements.

Quality of the included studies

To appraise the quality of the included articles we used the Joanna Briggs Institute (JBI) quality appraisal tool adapted for studies reporting prevalence data, cross-sectional and case-control studies (40). The following items were used to appraise cross-sectional studies: [1] inclusion criteria; [2] description of study subject and setting; [3] valid and reliable measurement of exposure; [4] objective and standard criteria used; [5] identification of confounder; [6] strategies to handle confounder; [7] outcome measurement; and [8] appropriate statistical analysis. In addition, JBI Systematic Reviews checklist for case control studies (41) using ten items were used to appraise one case control study (42). Studies considered low risk whenever fitted to 50% and or above quality assessment checklist criteria's (40,43). Using the aforementioned quality appraisal tools, no study was excluded (Table 1).

Data analysis

Data extraction were compiled using Microsoft Excel format and analyzed using STATA version 15 statistical software. Heterogeneity across studies was checked using the inverse variance (I^2) and Cochran Q statistics and the cut-offs of 25%, 50%, and 75% were used to declare the heterogeneity as low, moderate, and severe respectively (44,45).

As the preliminary output of the test statistics revealed a significant heterogeneity among studies (I^2 > 70%, P< 0.05), a random effects model was used to estimate the pooled prevalence of Cervical cancer (CC) with 95% confidence interval (CI). Subgroup analysis was also performed among regions and Human Immuno Virus (HIV) status in relation to outcome variable. Funnel plot, Egger and Begg tests at 5% significant level were employed to assess publication bias (46,47).

Results

Description of the identified studies

Until October 10, 2019 we identified a total of 109 articles using different data bases and University research repository. Sixty one (55.9%) of these identified articles were excluded because of similarity and duplication. Among the remaining 48 articles, 27 articles were excluded because the outcome was not clearly measured. Six articles were excluded due to exclusion criteria. Finally, 15 studies fulfilled the eligibility criteria and included in the final systematic review and meta-analysis (Figure 1).

Overview of included studies

Among the total 15 studies included to the current review, five of them were from Addis Ababa City Administration (17,42,48–50). Five studies were included from the Southern Nations Nationalities and People Region (SNNPR) (51–55). Except one study (42), all the rest included studies were conducted using cross sectional study design. Most of the studies used VIA as the measure of assessment tool for the outcome variable. The total participants in the included studies were 25,348 with sample ranged from 189 to 16,632. The response rate of all the included studies were greater than 90% and the quality score of the studies ranged from 62.5 to 100% (Table 2).

Publication bias

To assess publication bias, both the funnel plot and the Egger's test was conducted in the meta-analysis. The visual examination of the funnel plot exhibited a symmetric distribution of studies (Figure 2). In addition to the funnel plot, Egger's regression test was (β = -0.0061, SE=0.07, P=0.87) showed that no evidence of publication bias for the included studies.

Prevalence of Cervical Lesion

Fifteen studies with a total sample size of 25348 study subjects were included to the current review. From these, the lowest and the highest prevalence were found to be 1.56% (48) and 28.4% (17). The lowest prevalence was reported from SNNPR whereas the highest prevalence were reported from a studies done in Addis Ababa. Overall, the pooled prevalence of cervical lesion in Ethiopia was 16.36 (95 CI: 10.97-21.75) (Figure 3).

Since the I^2 static test for heterogeneity indicated that the studies differed significantly (I^2= 96.0%, p< 0.05) and because theoretically we expected differences among studies due to different reasons, we fitted a DerSimonian and Laird random effect model (61,62) to estimate the pooled prevalence of cervical lesion. Studies that showed the largest weight were Plezer et al (48) that showed 7.12 and Tadesse B. et al (59) that showed 6.80 weight. Whereas Birara et al showed a relatively smaller weight which is 6.45 (Figure 3).

The sub-group analysis by region showed the highest pooled prevalence of cervical lesion was found in SNNPR, 19.65% (95% CI: 15.51 – 23.80) followed by Addis Ababa City Administration in which the pooled prevalence was 15.10 (95% CI: 4.77-25.44).

In addition, sub-group analysis was done using HIV status of study participants. The highest pooled estimate of cervical lesion was found in those study participants whose sero-status is unknown, 17.27 (95% CI: 5.12-29.41). Whereas the pooled prevalence cervical lesion of those study participants whose status was confirmed to be positive was 15.27 (95% CI: 9.06 – 21.48) (Table 3).

The sub-group analysis showed as there is presence of heterogeneity across the studies. Hence, to identify the source of heterogeneity, we conducted meta-regression and sensitivity analysis. The meta-regression analysis was conducted using the following study covariates: publication years, HIV status, sample size, and study area. However, the results showed that none of these variables were a statically significant source of heterogeneity. We also carried out sensitivity analyses to observe the influence of each study on the overall effect size. No study significantly affected the overall pooled estimate of cervical lesion.

Meta-regression

Meta-regression was done to observe the trends of the prevalence of cervical lesion in Ethiopia using the reported prevalence and year of study. A significant upward trend in the prevalence of cervical lesion was observed from 1992 to 2018 (B =0.55, P=0.013) (Figure 4). However; there was no significant association between prevalence of cervical lesion and sample size of the included studies (B =−0.00023, P= 0.77).

Discussion

Cervical cancer ranks as the second most frequent cancer among women in Ethiopia. Awareness creation about the screening was being advocated in the country since 2008 (63). Despite this fact, very few women receive screening services (64). About 6,294 new cervical cancer cases are diagnosed annually in Ethiopia (estimates for 2018). Cervical cancer ranks as the 2nd leading cause of female cancer in Ethiopia (13).

The current systematic review and meta-analysis aimed in estimating the pooled prevalence of cervical lesion among Ethiopian women. The result reviled that the overall pooled prevalence of cervical lesion was 16.36% (95% CI: 10.97, 21.75). This finding is almost consistent with a study done in Rural Nigerian Women in which 16.6% had cervical lesion (65) and another study done in Tanzania (cross-sectional hospital-based, majority was HIV+) and Nigeria reveled 17% and 17.8% women had cervical lesion respectively (66,67).

This finding is higher than from a study done in Tanzania (systematic review) in which the overall prevalence of cervical lesion was 9.2% (68) and Zaria state Nigeria in which the overall prevalence of cervical lesion was 4.8 (69). Another study done in Kwara State, Nigeria (urban community) showed that 5% of study participants had cervical lesion (70). A community based screening in Turkey showed that a prevalence of 9.4% cervical lesion (71). A similar study in India on community-based cervical cancer screening program among women of Delhi obtained 4.67% cervical lesion (72).

The possible explanation for this discrepancy might be the mean age of marriage among the respondents in the aforementioned studies was relatively higher. As early marriage is one of the risk factor for having cervical lesion, this might augment the incidence and prevalence of the cervical lesion. The other explanation might be most of researches conducted in the aforementioned countries were from urban settings and they might have awareness and access to information this might lead them to have early screening for the disease.

This finding is lower than a study done in Senegal in which 21.03% of study participants had cervical lesion (73). Another study done in Nigeria among HIV Positive women showed that 22.2% of women had cervical lesion (74). The possible elucidation for such discrepancy between the current finding and other comparable study findings might be due to the difference in the Socio-demographic variations in the included study participants. A study from countries contained a data mostly collected mostly from the rural population and HIV positive women while in our study; both urban and rural settings were considered. The other possible explanation for the above variation could be due to the difference in study design.

Subgroup analysis

By region:

The highest pooled prevalence of cervical lesion was seen in Southern Nation and Nationalities and People's Region (SNNPR) which was 19.65%. This finding was higher compared to studies conducted in Addis Ababa and Amhara region that revealed 15.10% and 14.35% respectively. The possible explanations for this variation might be accounted by variations in information dissemination across the regions for reproductive health women about the disease. Hence, those women who had not information might remain with the symptom/disease.

By HIV status:

It is known that HIV infection is one of the main risk factors for the development of cervical dysplasia. On this regard there are many reports on the association of HIV with increased risk of cervical dysplasia (67,74–76). However the current systematic

review and meta-analysis in the subgroup analysis revealed that the highest cervical lesion (17.27%) was found in those study participants whose sero-status was unknown. This finding might be supported by the WHO report that stated the likely pattern of cervical lesions expected in a previously unscreened population of women (77,78). In addition to this, the possible explanation for this finding might be accounted by participants who were not screened for HIV might be exposed for other risk factors for cervical cancer. Plus to this, though their sero-status were not known at the time of cervical lesion screening, they might be previously know that their sero-status for HIV/AIDS as positive.

Limitation:

In the current systematic review and meta-analysis, we noticed some limitations. The pooled prevalence was determined using 15 studies from four different administrative regions in Ethiopia. Hence, it might not represent the whole country as studies in more than half of the regions not included in the current review.

Conclusion

The current study revealed that one among six of the study participants had cervical lesion. The trend also showed that there is still an increased trend cervical lesion in the country. Though it is late, Ethiopia launched HPV vaccine last year December 2018. This will play a great role in the fighting against the high prevalence of the disease. Awareness creation programs should be done using various social Medias. In addition, best practices in achieving high vaccination coverage shall be adapted from other successful countries.

Abbreviations

CC: ———————————— Cervical cancer

CI: ———————————— Confidence Interval

HIV: ———————————— Human Immuno Virus

HPV: ————————————Human Papilloma Virus

VIA: ———————————— Visual Inspection with Acetic Acid

VILI: ———————————— Visual Inspection with Lugol’s Iodine

SNNPR: ———————————— Southern Nations Nationalities and People Region

WHO: ———————————— World Health Organization

Declarations

Ethics approval and consent to participate: Not applicable

Consent for publication: Not applicable

Availability of data and material: All data are available in the manuscript.

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Authors' contributions:

AS conceived and designed the research protocol. AS, TD and YB searched the studies and extracted all necessary data. GD, AE and YW checked the data extraction process. AS and TD led the revision and editing the manuscript and all the authors YB, GD, AE, BZ, EA and WA involved in revising and editing the final version of the manuscript. All authors have read and approved the final draft of the manuscript.

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Tables

Table 1: Critical appraisal result of the included studies, 2019

Included articles	Criterion No (items included to appraise cross-sectional and case control studies).										
	1	2	3	4	5	6	7	8	9	10	%
Pelzer et al.	ü	X	ü	ü	X	X	ü	ü	NA	NA	62.5
Awoke et al.	ü	ü	ü	ü	ü	ü	ü	ü	NA	NA	100
Hirut T et al.	ü	ü	ü	ü	ü	ü	X	ü	ü	ü	90
Terefu T. et al.	ü	ü	ü	ü	ü	ü	ü	ü	NA	NA	100
Abel G. et al.	ü	ü	ü	ü	ü	ü	ü	ü	NA	NA	100
Zewdie M. et al.	ü	ü	ü	ü	ü	ü	ü	ü	NA	NA	100
Tesfahun H. et al.	ü	ü	ü	ü	ü	X	ü	ü	NA	NA	87.5
Meseret A.& Tadiwos M.	ü	ü	ü	ü	ü	ü	ü	ü	NA	NA	100
Melkamu G et al.	ü	ü	ü	ü	ü	ü	ü	ü	NA	NA	100
Tadesse B et al.	ü	ü	ü	X	ü	ü	X	ü	NA	NA	75
Limenih S. et al.	ü	ü	ü	ü	ü	ü	ü	ü	NA	NA	100
Sami-Ramzi L. et al.	ü	ü	ü	ü	ü	ü	ü	ü	NA	NA	100
Netsanet S. et al.	ü	ü	ü	ü	ü	ü	ü	ü	NA	NA	100
Ruland et al.	ü	ü	ü	ü	X	X	ü	ü	NA	NA	75
Birra B.	ü	ü	ü	X	ü	ü	ü	ü	NA	NA	87.5
√ = criterion fulfilled, X = criterion not fulfilled NA = not applicable											

Table 2: Characteristics of the included studies in the review and meta-analysis, Ethiopia, 2019

rs e	Study Year	Region	Method of assessment	HIV Status	Study design	Mean age	Response rate(%)	Sample size	Total N outcome	Prevalence (%)	Quality Score
et	1992	Addis Ababa	cytological investigation	Unkown	Cross-sectional	NR	90%	2111	33	1.56	62.5
e	2017	Amhara	VIA	Both	Cross-sectional	35	100%	428	61	14.3	100
et	2016	Addis Ababa	VIA	Both	Case control	39.87	95%	360	46	12.8	90
T. 1)	2017	SNNPR	women's chart	Both	Cross-sectional	NR	100%	528	146	27.7	100
et	2013	SNNPR	VIA	HIV	Cross-sectional	33	98%	448	99	22.1	100
.	2013	Oromia	VIA	Both	Cross-sectional	32.4	100.00%	334	43	12.9	100
un	2010	SNNPR	Diagnosis logbook	Both	Cross-sectional	41.6	91.70%	2120	350	16.5	87.5
t s	2015	Addis Ababa	VIA	Unkown	Cross-sectional	35.7	99%	226	54	24.1	100
nu	2014	Amhara	Pap stain	Both	Cross-sectional	35.02	97.80%	400	56	14.1	100
e	2018	Amhara	Pap smear	HIV	Cross-sectional	34.48	97.60%	284	28	9.9	75
n	2015	Amhara	women's chart	HIV	Cross-sectional	35.9	100.00%	435	88	20.2	100
4)	2006	SNNPR	VIA	Unkown	Cross-sectional	NR	100.00%	537	93	17.3	100
et	2014	Addis Ababa	VIA	HIV	Cross-sectional	NR	100%	16632	1663	10	100
et	2006	SNNPR	Digene HPV test	Unkown	Cross-sectional	34	100%	189	30	15.9	75
	2016	Addis Ababa	VIA	Unkown	Cross-sectional	35.73	99%	316	89	28.4	87.5

Table 3: Subgroup analysis showing the prevalence of cervical lesion among Ethiopian regions, 2019.

Variables	Region/city administration	Number of studies	Sample size	Estimate (95%CI)
By region	Addis Ababa	5	19645	15.10 (4.77, 25.44)
	SNNPR	5	3822	19.65 (15.51, 23.80)
	Amhara	4	1547	14.35 (10.27, 18.42)
	Other*	1	334	12.90 (7.89, 17.91)
By HIV Status	Unknown/Undiagnosed	5	3379	17.27 (5.12, 29.41)
	Both (HIV+ & HIV-)	6	4170	16.08 (12.13, 20.03)
	HIV+	4	17799	15.27 (9.06, 21.48)
Over all		15	25348	16.36 (10.97, 21.75)

Figures

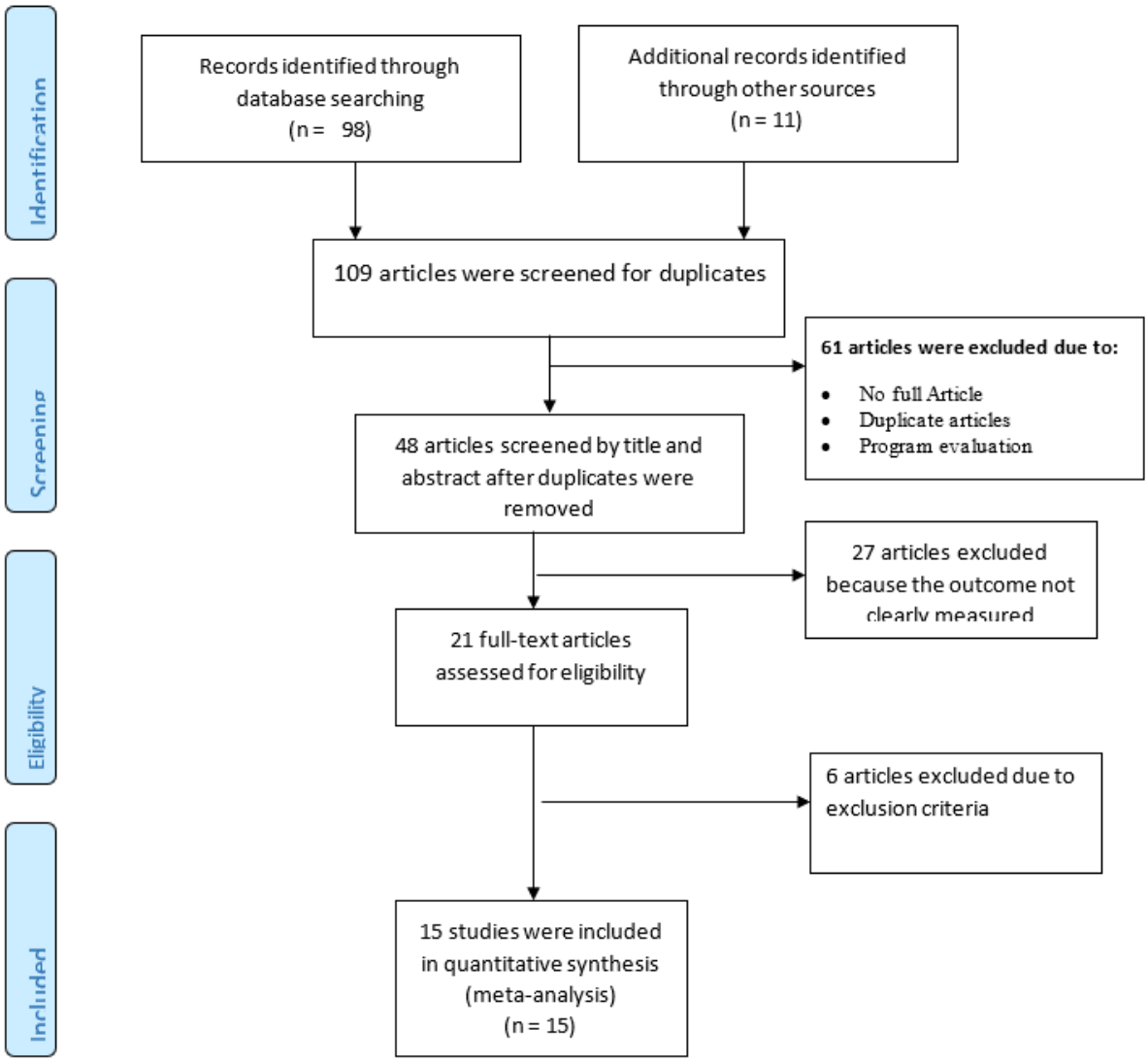

Figure 1

PRISMA Flow diagram showing the selection of studies for a systematic review and meta-analysis, 2019.

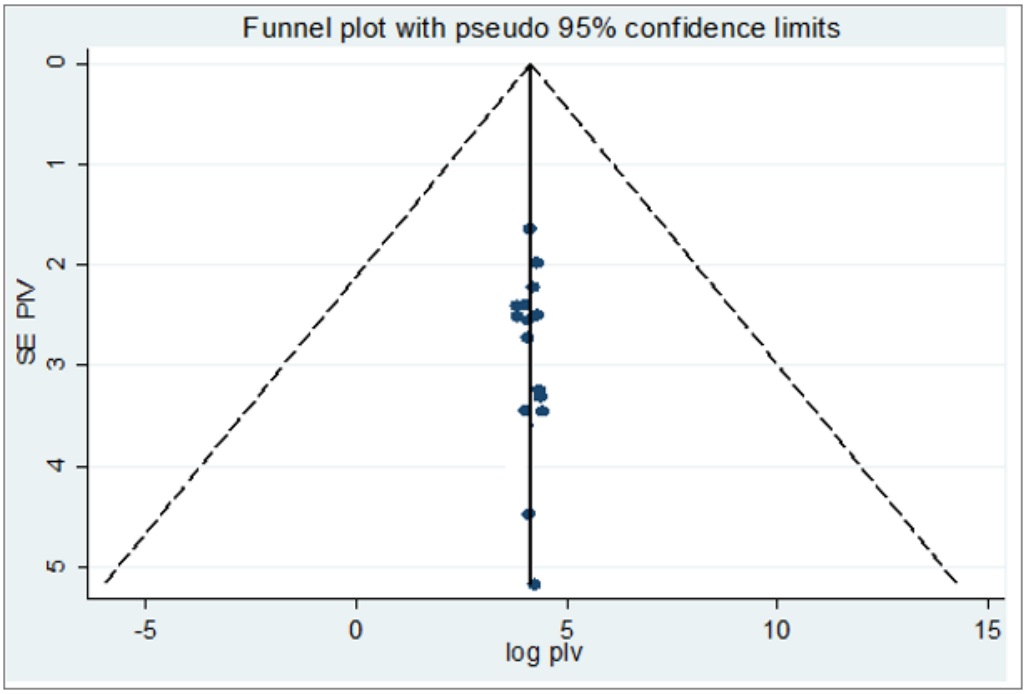

Figure 2

Funnel plot presentation to assess publication bias for the burden of cervical lesion among studies conducted in Ethiopia, 2019.

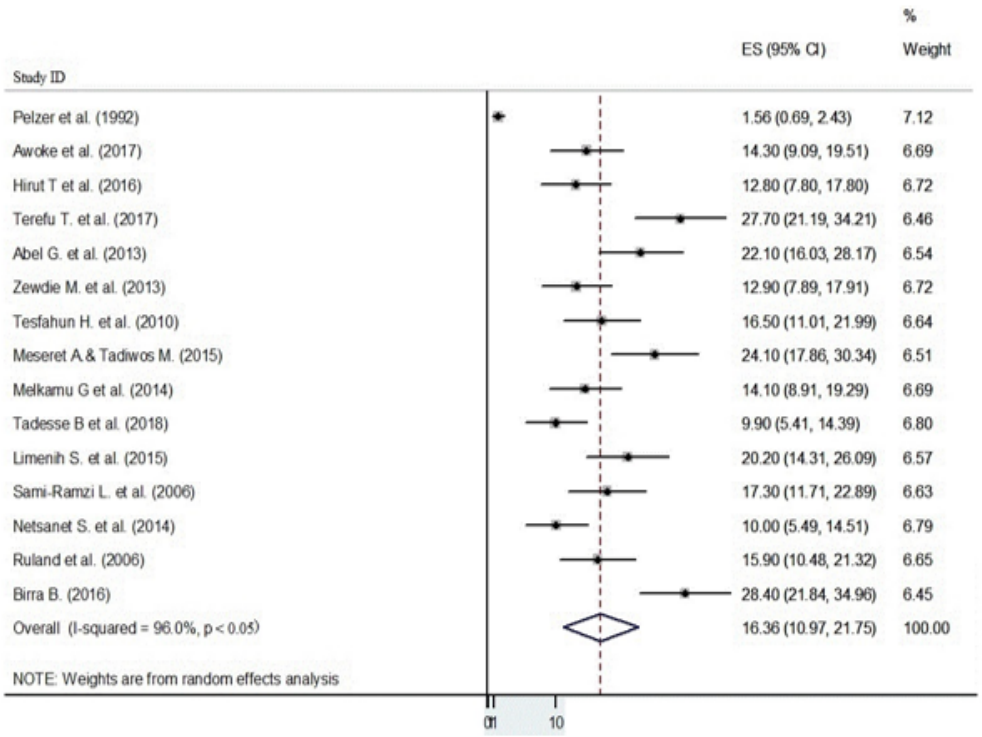

Figure 3

Over all pooled prevalence of cervical lesion in Ethiopia, 2019.

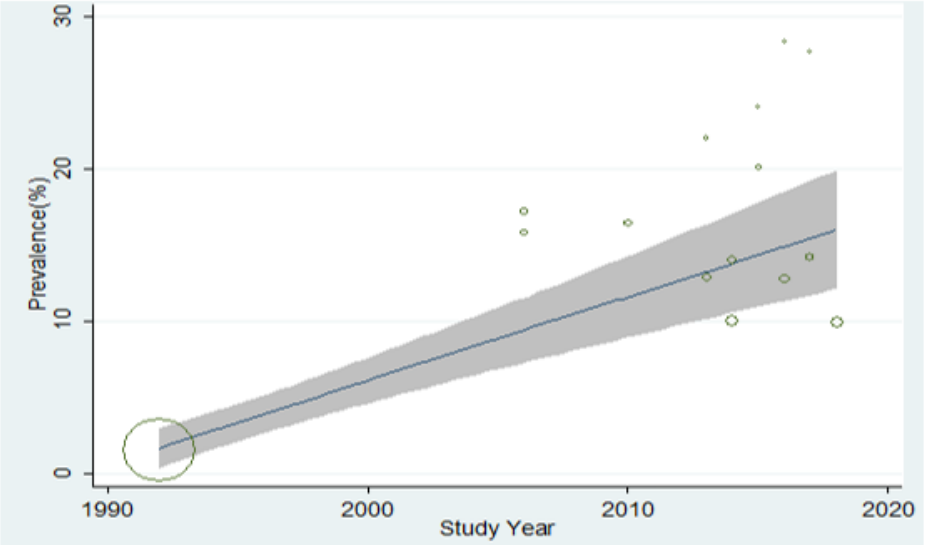

Figure 4

Meta-regression of the prevalence of cervical lesion by year of study (B = 0.55,P = 0.013)