BMJ Paediatrics Open

Congenital anomalies and risk factors in Africa: a systematic review and meta-analysis

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To cite: Moges N, Anley DT, Zemene MA, *et al*. Congenital anomalies and risk factors in Africa: a systematic review and meta-analysis. *BMJ Paediatrics Open* 2023;**7**:e002022. doi:10.1136/bmjpo-2023-002022

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/bmjpo-2023-002022).

Received 11 April 2023
Accepted 22 June 2023

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ABSTRACT

Objective To evaluate the pooled prevalence and identify risk factors of congenital anomalies among neonates in Africa.

Methods The pooled birth prevalence of congenital anomalies was the first outcome of this review, and the pooled measure of association between congenital anomalies and related risk factors in Africa was the second. We conducted a thorough search of the databases PubMed/ Medline, PubMed Central, Hinary, Google, Cochrane Library, African Journals Online, Web of Science and Google Scholar up to 31 January 2023. The JBI appraisal checklist was used to evaluate the studies. STATA V.17 was used for the analysis. The I^2 test and Eggers and Beggs tests were used to measure study heterogeneity and publication bias respectively. The pooled prevalence of congenital anomalies was calculated using DerSimonian and Laird random-effect model. Subgroup analysis, sensitivity analysis and meta-regression were also performed.

Result This systematic review and meta-analysis includes 32 studies with a total of 626 983 participants. The pooled prevalence of congenital anomalies was 23.5 (95% CI 20 to 26.9) per 1000 newborns. Not taking folic acid (pooled OR=2.67; 95% CI (1.42 to 5.00)), history of maternal illness (pooled OR=2.44, 95% CI (1.2 to 4.94)), history of drug use (pooled OR=2.74, 95% CI (1.29 to 5.81)), maternal age (>35 years.) (Pooled OR=1.97, 95% CI (1.15 to 3.37)), drinking alcohol (pooled OR=3.15, 95% CI (1.4 to 7.04)), kchat chewing (pooled OR=3.34, 5% CI (1.68 to 6.65)) and urban residence (pooled OR=0.58, 95% CI (0.36 to 0.95)) were had significant association with congenital anomalies.

Conclusion The pooled prevalence of congenital abnormalities in Africa was found to be substantial, with significant regional variation. Appropriate folate supplementation during pregnancy, proper management of maternal sickness, proper antenatal care, referring healthcare personnel before using drugs, avoiding alcohol intake and kchat chewing are all important in lowering the occurrence of congenital abnormalities among newborns in Africa.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Congenital anomaly is defined as structural or functional abnormalities that occur during intrauterine life and can be identified prenatally, at birth, or sometimes may only be detected later in infancy. Congenital anomalies are one of the main causes of the global burden of disease.

WHAT THIS STUDY ADDS

⇒ There was significant regional variation in the prevalence of congenital anomalies. Kchat chewing, ingestion of alcohol or drugs and not taking folic acid were all risk factors for pregnant women having congenital anomalies.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Improvements in education and antenatal care to pregnant women can reduce the risk of congenital anomalies. Focusing on primary healthcare, especially in rural areas may help reduce the risk of congenital anomalies.

INTRODUCTION

According to WHO, congenital anomaly is defined as structural or functional abnormalities that occur during intrauterine life and can be identified prenatally, at birth, or sometimes may only be detected later in infancy. Congenital anomalies are one of the main causes of the global burden of disease. An estimated 240 000 newborns die worldwide within 28 days of birth every year due to congenital disorders. In addition, ccongenital disorders cause a further 170 000 deaths of children between the ages of 1 month and 5 years.[1]

It has been estimated that about one-quarter of all congenital anomalies might have a genetic cause. The two most common genetic causes of congenital anomalies are single-gene defects and chromosomal abnormalities.[2]Single-gene defects are caused by changes (mutations) in the structure of genes. These are responsible for slightly over 17% of congenital anomalies.[3] Abnormalities caused by chromosomal changes

are identified in about 10% of children with congenital anomalies[3] and might involve the autosomes or the sex chromosomes. Identified environmental and maternal causes are responsible for an estimated 4%–10% of congenital anomalies.[4]

According to severity, congenital anomalies are categorised in to major and minor abnormalities.[5] Moreover, they can be divided into three categories: minor, severe and lethal anomalies. Major anomalies are those that are both severe and lethal.[6] However, the worldwide classification of disorders categorised CAs according to the body system that was impacted.[7]

An estimated 7.9 million children every year, or 6% of all births globally, are projected to have a significant birth abnormality that is entirely or partially genetic. Further, hundreds of thousands more children are born with severe birth defects that developed after conception as a result of maternal exposure to environmental toxins (teratogens) that can harm an unborn child, including alcohol, rubella, syphilis and iodine deficiency.[8 9]

According to a conservative estimate, birth malformations are responsible for approximately 3.3 million deaths annually. This estimate takes into account both the 50% of infants who pass away in low-income nations and the 30% of high-income and middle-income countries who are born with major birth defects that are largely or entirely genetic in nature. A further 3.2 million infants each year who are born with a significant birth defect are predicted to become impaired in the absence of adequate treatment[8 9]

Although birth abnormalities are a worldwide issue, they have a disproportionately negative impact in middle-income and low-income nations, where they account for almost 94%t of major birth defect births and 95%t of these children's deaths. For instance, the prevalence of congenital anomalies in Egypt, Ethiopia, Kenya, Uganda and Nigeria[10–14] is higher than the prevalence in India, Iran and British.[15–17] Due to stark differences in maternal health and other significant risk factors, such as poverty, a high percentage of older mothers, a higher frequency of consanguineous marriages, and the survival advantage against malaria for carriers of sickle cell, thalassaemia and glucose-6-phosphate dehydrogenase, both the proportion of births with birth defects and the absolute number of births are much higher in middle-income and low-income countries than in high-income countries.[18–21]

Although there are many variations, countries with middle-income and low-income levels often have higher birth prevalences of postconception birth abnormalities caused by teratogens. They are less likely to have methods to identify diseases brought on by such exposure, and it is difficult to quantify such issues. As a result, they frequently have few, if any, laws governing the use of some of these chemicals, and their health services are rarely focused on recognising and limiting exposure. Every year, an undetermined number of infants with severe birth abnormalities caused by teratogens are surely born, most likely in the hundreds of thousands.[22 23]

Unfortunately, due to a lack of information from the National Birth Defect Registry, there are not enough reports on the prevalence and risk factors of congenital malformations in African nations. African newborns' overall prevalence of birth abnormalities and associated risk factors have not yet been studied.

The aim of this systematic review and meta-analysis was to estimate the pooled prevalence of congenital anomalies in African countries and to identify the associated risk variables.

METHODS

Reporting of the findings and review registration

Preferred Reporting Items for Systematic Reviews and Meta-Analyses statements were used to report the current systematic review and meta-analysis[24] (online supplemental file 1). The review protocol has been registered in PROSPERO with the registration ID of CRD42023393503.

Search strategies

Up until 31 January 2023, the following databases were systematically searched for pertinent studies: PubMed/Medline, PubMed Central, Hinary, Google, Cochrane Library, African Journals Online, Web of Science and Google Scholar. Reference lists of identified articles were also browsed. The primary search was performed in an advanced PubMed database, using Medical Subject Heading terms. The core search terms and phrases were considered interchangeably in different databases. Moreover, grey literature was retrieved using Google and Google Scholar searches (online supplemental file 2).

Eligibility criteria

Published and unpublished, full text, articles at any study period and study design that report the prevalence of congenital malformations or at least one risk factor were included. The review did not include case reports, conferences, editorials, anonymous reports or research with restricted access (after two emails to the corresponding author). Also, if the total number of cases and births included in the study was not stated explicitly, the study was disqualified.

Review outcomes

The pooled prevalence of congenital abnormalities at birth was the study's initial finding. The combined assessment of congenital abnormalities and related risk factors in Africa was the second outcome. The number of congenital anomalies cases in live births and/or stillbirths at birth divided by the overall number of births (live births and/or stillbirths) during the research period is known as the birth prevalence of congenital anomalies.

Quality assessment

The Joanna Briggs Institute (JBI) quality appraisal checklist was used to evaluate the quality of each study.[25] The JBI critical appraisal checklist (which has nine items) was adapted for the studies reporting the prevalence data

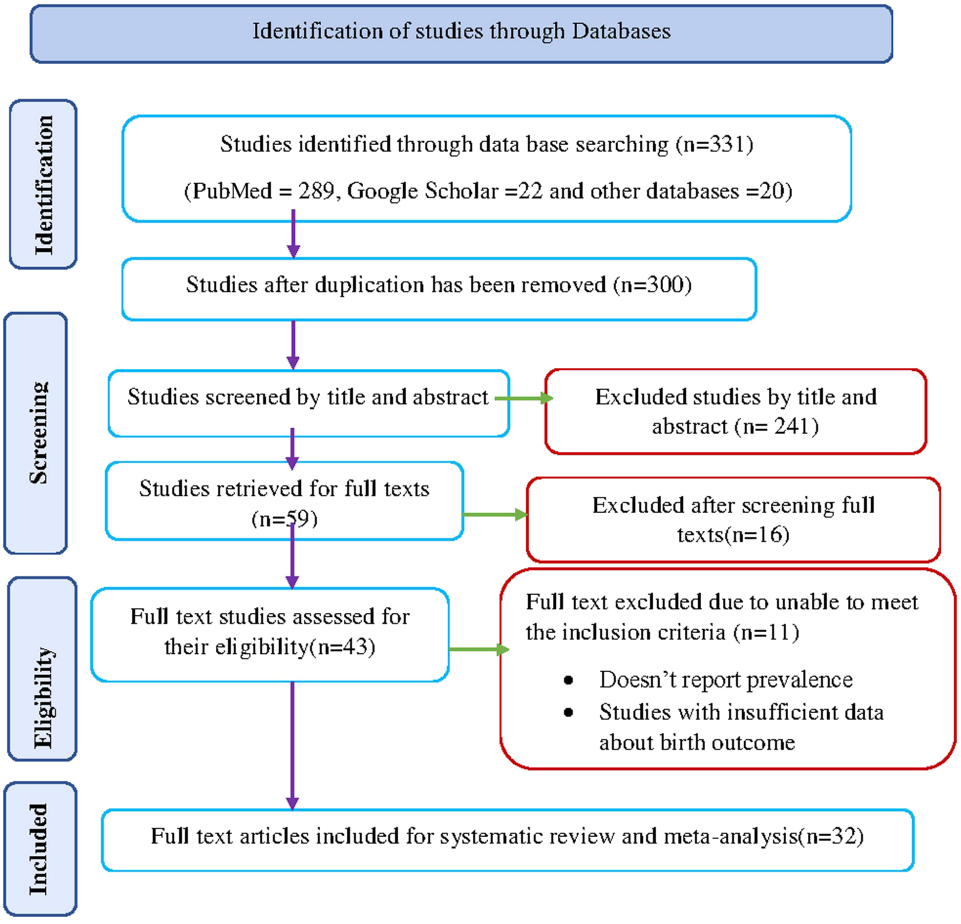

Figure 1 Study selection flow diagram; a figure adapted from the PRISMA group statement for thi review. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

(online supplemental file 3). Using the framework, three reviewers (NM, DT and AMM) independently evaluated the quality of each study. During the evaluation of quality, disagreements between reviewers were resolved by using the average score of the three reviewers. In the end, if the study received five or more points on all quality assessment items, it was deemed low risk.[26]

Study selection and data abstraction

EndNote V.21 software reference manager was used to remove duplicate studies after getting them all from the databases. On the basis of the title and abstract, the reviewers then selected the research for inclusion. After carefully reviewing the full text studies and incorporating the qualified studies, three reviewers (NM, DT and AMM) separately retrieved all relevant data using a predefined data extraction template. The prespecified format reduced the likelihood of a reviewer's having a conflict of interest throughout the data extraction process, but if one did arise, the conversation was used to address the concerns. The study's principal author was contacted as needed.

First author, sample size, study nation, duration, study design, publication year, prevalence period, birth outcome, birth prevalence of congenital abnormalities and related risk factors were all included in the data extraction format (OR with CI of the variables were considered based on the available literatures). To preserve uniformity, prevalence reports from all studies in the various denominators have been translated to per 1000 births. After then, per 1000 prevalence numbers were employed to report the review's conclusions. Supplemental folic acid, place of residence, and mother age, history of maternal disease, use of unknown drugs, drinking alcohol, khat chewing, follow-up for antenatal care, and smoking were evaluated variables.

Meta analysis

The data were taken out of Microsoft Excel and exported to STATA V.17 Statistical Software for further analysis. To maintain uniformity, the prevalence was calculated per 100 births for each study.

The statistical heterogeneity between studies was examined using the I^2 statistic, and heterogeneity was visualised using a forest plot.[27] This demonstrated significant study heterogeneity (I^2=99.62%). Thus, a random-effect meta-analysis technique was used to ascertain the pooled prevalence of congenital anomalies.[28 29] Based on specific characteristics (study nation, study design, birth outcome, folic acid fortification status, epidemiological design and birth status), subgroup analysis was carried out. To determine the impact of a single study on the

Table 1 The characteristics of articles included in systematic review and meta-analysis 2023

Firtst author	Year	Country	Study design	Sample size	Cases	Duration/months	Prevalence/1000
Elawady[12]	2021	Egypt	Cross-sectional	1000	74	9	74
Birhanu[11]	2021	Ethiopia	Cross-sectional	422	78	4	185
Gedamu[40]	2021	Ethiopia	Cross-sectional	2218	23	19	1
Geneti[41]	2021	Ethiopia	Cross-sectional	45 951	253	60	5.5
Jemal[43]	2021	Ethiopia	Case control	418	-	6	-
Mekonen[46]	2021	Ethiopia	Cross-sectional	12 225	383	12	31.3
Mekonnen[47]	2020	Ethiopia	Case control	423	-	12	-
Mekonnen[48]	2021	Ethiopia	Cross-sectional	11 177	69	72	6.2
Silesh[55]	2021	Ethiopia	Cross-sectional	3346	199	1	59.5
Tsehay[57]	2019	Ethiopia	Case control	398	-	24	-
Abebe[32]	2021	Ethiopia	Case control	35 080	251	36	7.2
Getachew[42]	2022	Ethiopia	Cross-sectional	754	31	2	41.1
Seyoum[54]	2018	Ethiopia	Cross-sectional	19 650	317	36	16.1
Mombo[49]	2017	Gabon	Retrospective	7712	32	31	4.1
Wagathu[14]	2019	Kenya	Cross-sectional	315	61	1	193.7
Agot[33]	2020	Kenya	Cross-sectional	299 854	362	60	1.2
Ajao[34]	2019	Nigeria	Cross-sectional	1057	67	36	63.4
Anyanwu[35]	2015	Nigeria	Cross-sectional	1456	41	9	28.2
Bakare[36]	2009	Nigeria	Cross-sectional	624	43	12	68.9
Chukwubuike[37]	2020	Nigeria	Prospective	9492	166	36	17.5
Ekanem[39]	2011	Nigeria	Retrospective	39 693	125	168	3.1
Obu[50]	2012	Nigeria	Cross-sectional	607	17	60	28
Oluwafemi[51]	2019	Nigeria	Cross-sectional	8307	39	15	4.7
Onankpa[52]	2014	Nigeria	Prospective	1165	24	24	20.6
Adeboye[10]	2016	Nigeria	Prospective	396	44	12	111
Venter[58]	1995	South Africa	Prospective	10 380	234	48	22.5
Delport[38]	1995	South Africa	Prospective	17 351	206	48	11.9
Saib[53]	2020	South Africa	Retrospective	7516	117	12	15.6
Kishimba[44]	2015	Tanzania	Case control	412	-	24	-
Mumpe-Mwanja[13]	2019	Uganda	Cross-sectional	69 766	461	36	66.2
Singh[56]	2000	Libya	Cross-sectional	16 186	151	12	9.3
Kouame[45]	2015	cote d Ivoire	Cross-sectional	1632	1725	132	0.1

meta-total analysis's estimate, a sensitivity analysis was conducted. To pinpoint the cause of heterogeneity, meta-regression analysis was taken into consideration.

Assessment of publication bias

Funnel plot was used to depict the publication bias graphically. Statistics from the Egger's regression test and the Begg's test were used to formally identify publication bias.[30 31] As a result, publication bias was defined as a $p<0.05$.

Patient and public involvement

This study does not involve human participants.

RESULTS

Study selection

Initial searches on PubMed, Google Scholar and other databases turned up 311 papers on the prevalence and risk factors of congenital abnormalities. Thirty-one of them were eliminated as a result of duplicate articles.

Table 2 Study period, setting, birth outcome and quality of included studies in systematic review and meta-analysis 2023

First author	Prevalence period	Birth outcome	Study setting	Study quality
Elawady[12]	2017–2018	LB	Hospital based	Low risk
Birhanu/[11]	2020	LB	Hospital based	High risk
Gedamu[40]	2018–2019	LB	Hospital based	Low risk
Geneti[41]	2011–2015	LB+SB	Hospital based	Low risk
Jemal[43]	2020	LB	Hospital based	Low risk
Mekonen[46]	2018–2019	LB+SB	Hospital based	Low risk
Mekonnen[47]	2018–2019	LB	Hospital based	Low risk
Mekonnen[48]	2009–2014	LB	Hospital based	Low risk
Silesh[55]	2017–2019	LB	Hospital based	Low risk
Tsehay[57]	2017–2018	LB	Hospital based	Low risk
Abebe[32]	2016–2018	LB+SB	Hospital based	Low risk
Mombo[49]	2013–2015	LB+SB	Hospital based	Low risk
Wagathu[14]	____	LB	Hospital based	High risk
Agot[33]	2014–2018	LB	Hospital based	Low risk
Ajao[34]	2012–2016	LB	Hospital based	Low risk
Anyanwu[35]	2013	LB	Hospital based	Low risk
Bakare[36]	2003–2004	LB	Hospital based	Low risk
Chukwubuike[37]	2015–2018	LB	Hospital based	Low risk
Ekanem[39]	1990–2003	LB	Hospital based	Low risk
Obu[50]	2007–2011	LB	Hospital based	Low risk
Oluwafemi[51]	2014–2015	LB	Hospital based	Low risk
Onankpa[52]	2011–2012	LB	Hospital based	Low risk
Adeboye[10]	2009–2010	LB	Hospital based	Low risk
Venter[58]	1989–1992	LB	Hospital based	Low risk
Delport[38]	1986–1989	LB	Hospital based	Low risk
Saib[53]	2018	LB	Hospital based	Low risk
Kishimba[44]	2011–2012	LB	Hospital based	Low risk
Mumpe-Mwanja[13]	2015–2017	LB+SB	Hospital based	Low risk
Singh[56]	1995	LB+SB	Hospital based	Low risk
Kouame[45]	2000–2010	LB	Hospital based	Low risk
Getachew[42]	2018	LB+SB	Hospital based	Low risk
Seyoum[54]	2015–2017	LB+SB	Hospital based	Low risk

LB, live birth; SB, still birth.

After examining the titles and abstracts of the remaining 300 studies, 241 studies were eliminated as being unsuitable for this study. The remaining 59 studies' whole texts were read. The 32 studies that satisfied the inclusion criteria were included in this systematic review and meta-analysis[10–14 32–58] (figure 1).

Characteristics of original studies

The included studies were either cross-sectional (n=19), retrospective (n=3) or prospective studies (n=5) and case–control studies (n=5).[10–14 32–58] Of all studies, 12 were conducted in Ethiopia,[11 32 40–43 46–48 54 55 57] 9 in Nigeria,[10 34–37 39 50–52] 3 in South Africa,[38 53 58] 2 in Kenya,[14 33] 1 in Egypt,[12] 1 in Gabon,[49] 1 in Libya,[56] 1 in Uganda,[13] 1 in Tanzania[44] and 1 in Cote dIvoire.[45] All studies included in this review were published in the year between 1995 and 2022[10–14 32–58] (table 1). In addition, all articles were facility based (table 2).

Quality of the studies

All included studies had their quality assessed using JBI quality appraisal standards. The evaluation checklist for prevalence studies, which consists of nine questions and items with yes, no, unclear or not applicable responses, was used to assess 27 articles. The evaluation checklist for case control studies, which consists of ten questions and items with yes, no, unclear or not applicable responses, was used to assess the remaining five studies. The JBI

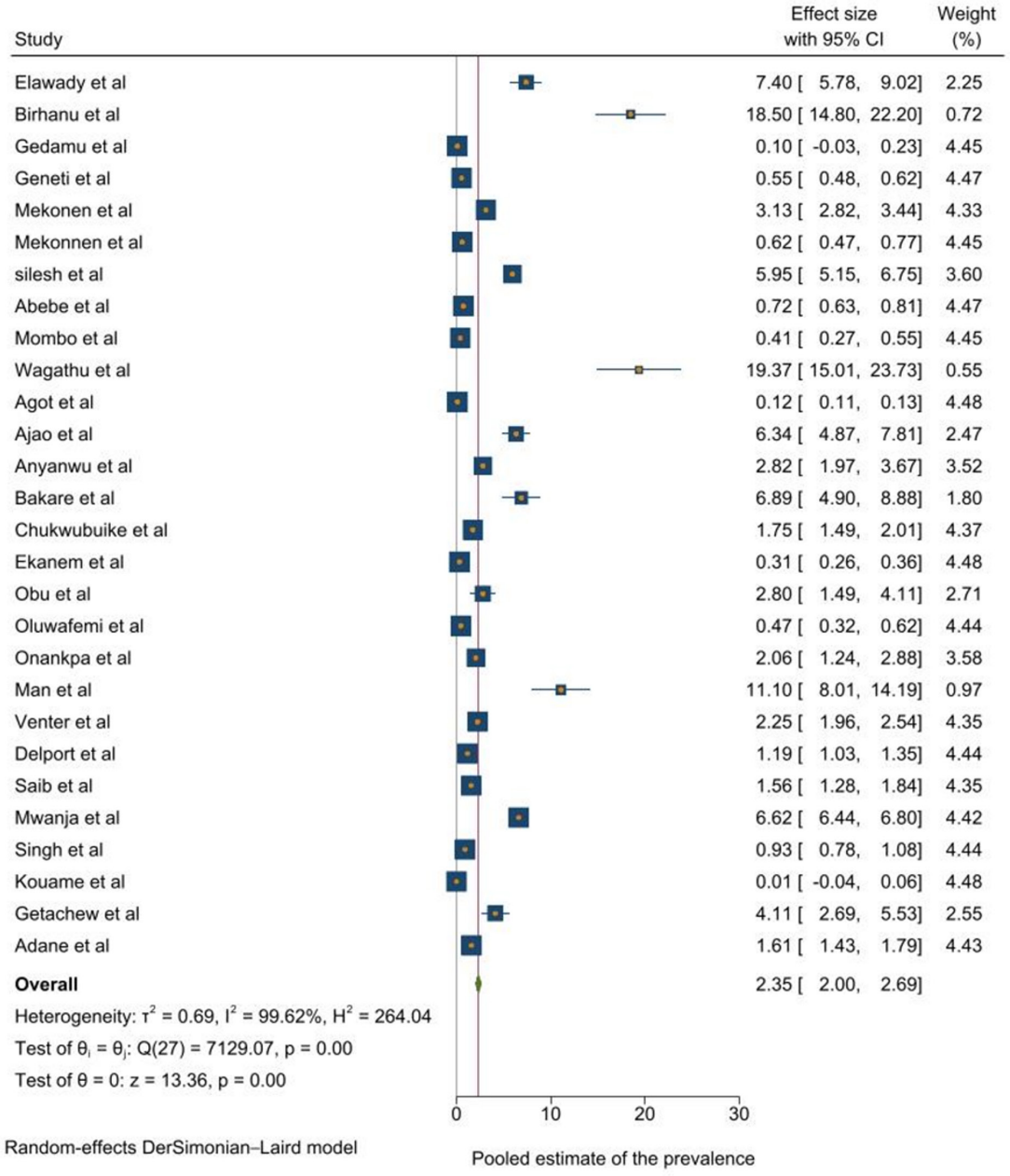

Figure 2 Forest plot showing prevalence of congenital anomalies in Africa, 2023.

descriptions for each item served as the basis for the quality assessment grade for all goods. The quality ratings of the studies ranged from four to nine as a consequence. Hence, none of the studies had a considerable chance of being of low quality, with the exception of two research that received four.[10–14 32–58] (online supplemental file 4).

Meta analysis

Prevalence of congenital anomalies

In the present meta-analysis, the pooled birth prevalence of congenital anomalies was 2.35% (or 23.5 per 1000 births) (95% CI 2% to 2.69%). A forest plot showed that there was statistically significant heterogeneity across the studies. Therefore, the random-effect meta-analysis model was applied to pool the overall prevalence of the studies (figure 2).

Subgroup analysis

Subgroup analysis based on the study country, study design and birth outcome were carried out to see the variation of the prevalence across the studies.

Subgroup analysis based on the study country was performed to see the pooled prevalence of each country in Africa. High pooled prevalence of congenital anomalies was detected in Kenya 9.62% (95% CI −9.25% to 28.48%), Egypt 7.4% (95% CI 5.78% to 9.02%), Uganda 6.62% (95% CI 6.44% to 6.8%), Nigeria 2.66% (95% CI 2.01% to 3.32%) and Ethiopia 2.12% (95% CI 1.6% to 2.64%) (table 3).

Table 3 The pooled prevalence of congenital anomalies among African countries

Country	Prevalence in % (95% CI)
Egypt	7.4 (5.78 to 9.02)
Ethiopia	2.12 (1.6 to 2.64)
Gabon	0.41 (0.27 to 0.55)
Kenya	9.62 (–9.25 to 28.48)
Libya	0.93 (0.78 to 1.08)
Nigeria	2.66 (2.01 to 3.32)
South Africa	1.66 (1.04 to 2.28)
Uganda	6.62 (6.44 to 6.8)
Cote dIvoire	0.01 (–0.04 to 0.06)
D+L pooled ES	2.35 (2 to 2.69)

D+L, Der Simonian and Laird; ES, effect size.

In the present review, statistically significant heterogeneity between countries was detected (p=0.001, I^2=99.62 %). Therefore, the Der Simonian and Laird's (D+L) pooled prevalence method was considered because it is more conservative than the inverse variance method. The difference between countries was significant (p<0.001).

Subgroup analysis based on study design, using the D+L method (p<0.001, I^2=99.62%), the prevalence of congenital anomalies for cross-sectional studies was 2.98% and for prospective studies was 2.21% (figure 3).

Subgroup analysis based on birth outcome was done to see the burden in live births only[50] and both live births and stillbirths (LB+SB). The pooled prevalence of congenital anomalies per live birth was 1.75% (95% CI 1.50% to 2.00%) and both live birth and stillbirth was 2.22% (95% CI 1.05% to 3.40%) (figure 4).

Meta-regression analysis

In this systematic review and meta-analysis, sample size (p=0.01), year of publication (p=0.05), duration of the study in months (p=0.00), study country (p=0.66), study design (p=0.01), birth outcome (p=0.46) were analysed for the source of heterogeneity. Sample size and study design were significant for the source of heterogeneity.

Sensitivity analysis

No study that has a unique impact over others on the evaluation of meta-analysis as a whole was found in this review (figure 5). In essence, CIs are consistent across research. While the heterogeneity between studies did not significantly decrease (p<0.001, I^2=99.62%) after performing the analysis with a small number of studies, sensitivity analysis does not help to explain heterogeneity. We also run leave-one-out analyses, but this did not appreciably lower the heterogeneity of the studies. By lowering the number of studies included in a meta-analysis, we performed sensitivity analysis to investigate the effect of low-quality studies on overall estimates. By only including high-quality papers with a score of greater than or equal to 5, we were able to determine the meta-analysis estimations. As a result, we obtained results that were similar to the earlier discovery, and the pooled estimate was 2.35% (95% CI 2% to 2.69%).

Publication bias

Publication bias was estimated using the Egger's regression tests (B-coefficient of bias: 7.3; p<0.001). A funnel plot showed an asymmetrical distribution (figure 6A,B). Additionally, the outcomes of the Egger and Begg tests revealed strong proof of publication bias (p<0.05). Trim-and-fill analysis was therefore carried out. The run L0 estimator was used to impute two trials, and the trim-and-fill analysis produced a pooled prevalence of 21.4 (95% CI 17.9 to 24.8) when the two studies were imputed.

Factors associated with congenital anomalies among neonates in Africa

In this meta-analysis and systematic review, factors such as folic acid supplementation, smoking, maternal illness, unidentified drug use, maternal age, antenatal care, alcohol, chat chewing and residence were all evaluated for their association to congenital anomalies. The summary of studies (pooled OR, CI, etc) is described in (table 4).

Nine studies found a significant association between folic acid supplementation and congenital anomalies. The odds of congenital anomalies among mothers with no folic acid supplementation range from 1.42 to 5.00.

Seven studies point out that the presence of maternal illness during pregnancy was associated with congenital anomalies among newborns (pooled OR=2.44, 95% CI (1.2 to 4.94)). This implies that neonates born from mothers who had illness during pregnancy is 2.44 times high likely to have congenital anomalies.

Six studies showed that history of drug use during pregnancy has a significant association with congenital anomalies (pooled OR=2.74, 95% CI (1.29 to 5.81)). This indicates neonate mother who took drug during pregnancy increase the risk of congenital anomalies by 2.74-fold.

Nine studies demonstrated that the odds of congenital anomalies among >35 years. Old mothers are 1.97 times higher compared with <35 years old moms (pooled OR=1.97, 95% CI (1.15 to 3.37)).

Six studies found a significant association between drinking alcohol and congenital anomalies. the odds of congenital anomalies were range from 1.4 to 7.04.

Four studies indicated that there is significant association between kchat chewing and congenital anomalies (pooled OR=3.34, 95% CI (1.68 to 6.65)). This implies newborn infants born from mothers, who are kchat chewers, are 3.34 times high likely to have congenital anomalies compared with their counterparts.

A significant association was detected between urban residence and congenital anomalies (pooled OR=0.58, 95% CI (0.36 to 0.95)). Newborn infants born from rural resident mothers are less likely to have congenital

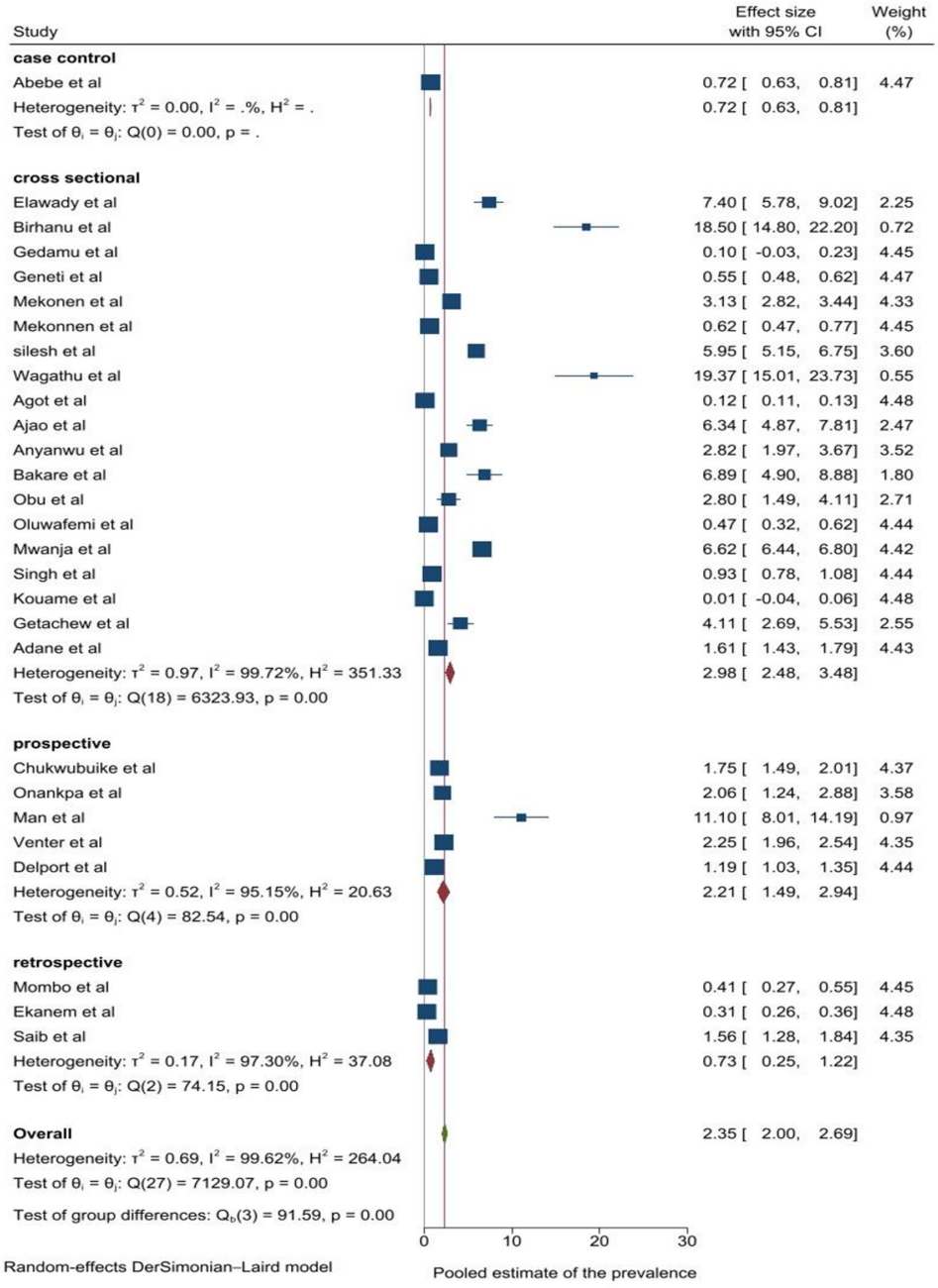

Figure 3 Subgroup analysis based on study desing in Africa.

anomalies by 42% as compared with born from urban resident mothers.

DISCUSSION

Identifying the pooled prevalence and risk variables of congenital abnormalities among newborns in Africa was the goal of this systematic review and meta-analysis. Congenital anomalies are a collection of newborn defects that develop during pregnancy. These illnesses, which can have seriously detrimental impacts on an infant's life and health, are categorised as structural or functional. This review revealed the pooled prevalence in Africa and it assessed risk factors (folic acid supplementation, smoking, maternal illness, unidentified drug use, maternal age, ante natal care, alcohol, kchat chewing and residence) for association with congenital anomalies.

The pooled prevalence of congenital anomalies among newborns in Africa was found 23.5% per 1000 births with the range of 20%–26.9%. Different prevalences have been reported by a study conducted in India,[15 59] Iran,[17] British,[16]Europe,[60] Lebanon[61] and worldwide.[1] Our study also demonstrated that there are considerable differences in prevalence among African countries. Subgroup analyses were conducted based on the study country, design and birth outcome. As a result, a considerable disparity in the occurrence of congenital anomalies in different African countries was revealed in this study. Kenya 9.62%, Egypt 7.4%, Uganda 6.62%, Nigeria 2.66%, Ethiopia

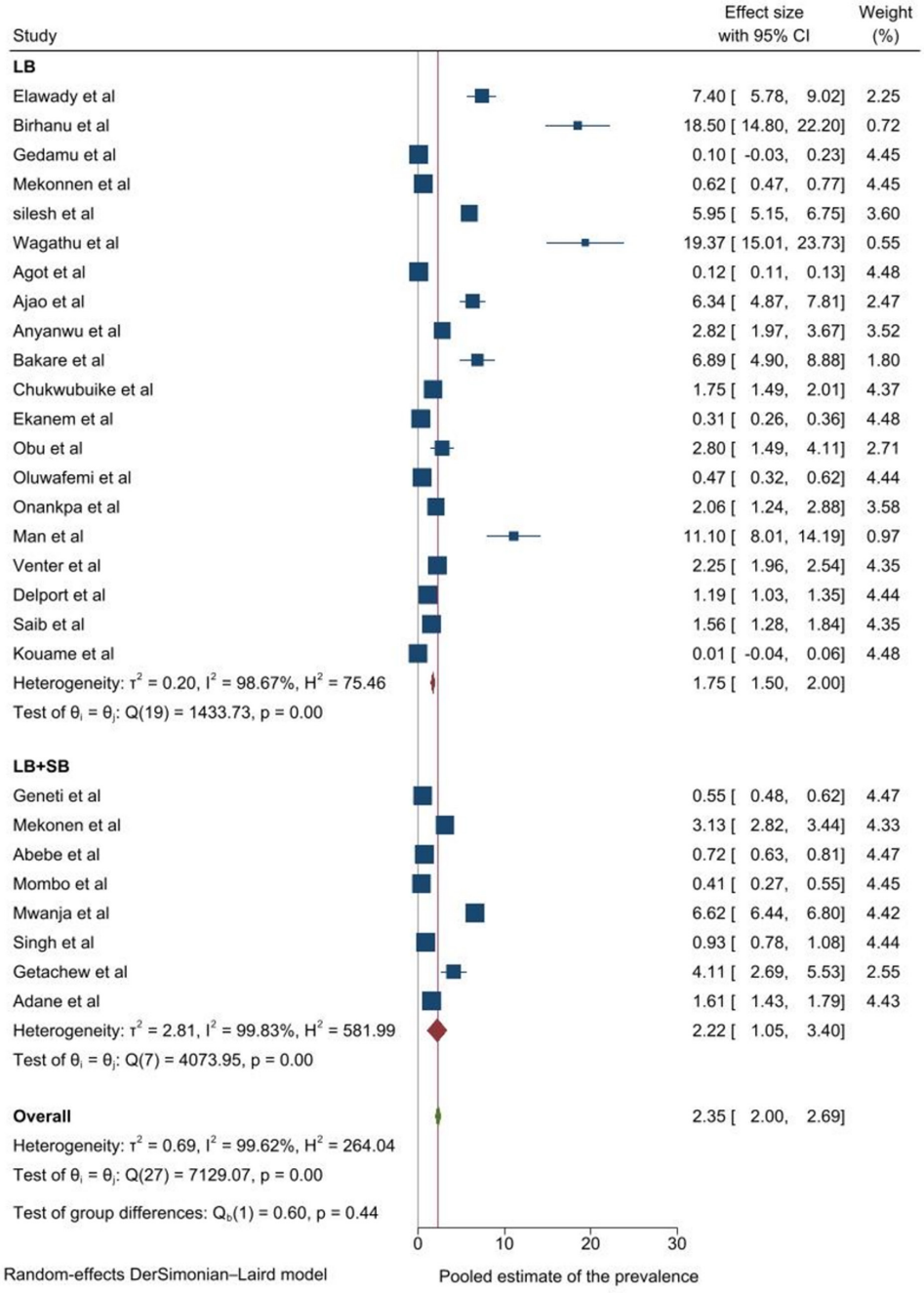

Figure 4 Subgroup analysis based on birth outcomes in Africa. LB, live birth; SB, still birth.

2.12% and south Africa 1.66% had a high prevalence of congenital anomalies. Of all, the highest and lowest rates were detected in Kenya and Cote d Ivoire, respectively.

In the present review, the pooled prevalence of congenital anomalies among newborns in Africa is comparable with the studies conducted in India,[15] Iran,[17] Europe,[60] Lebanon.[61] In addition, our finding is higher than the study conducted in British[16] and lower than the study conducted in Pakistan.[62]

The prevalence of congenital anomalies in low-income countries is significantly high. According to estimates, low-income and middle-income countries account for 94% of cases of severe congenital disorders. This may have occurred because pregnant women did not have access to enough healthy diets, they were exposed to more illnesses and alcohol, and they had less access to healthcare and screenings.[1]

In this study, there is a significant association between congenital anomalies and folic acid supplementation. The odds of congenital anomalies among mothers without folic acid supplementation are 2.67 times higher compared with mother supplemented with folic acid. This finding is supported by clinical evidence that folic acid (vitamin B_9) is an essential component needed for DNA replication as well as a variety of enzymatic processes related to vitamin and amino acid metabolism. Because folate is necessary for the fetus' growth and development, its demands rise throughout pregnancy. Anaemia and

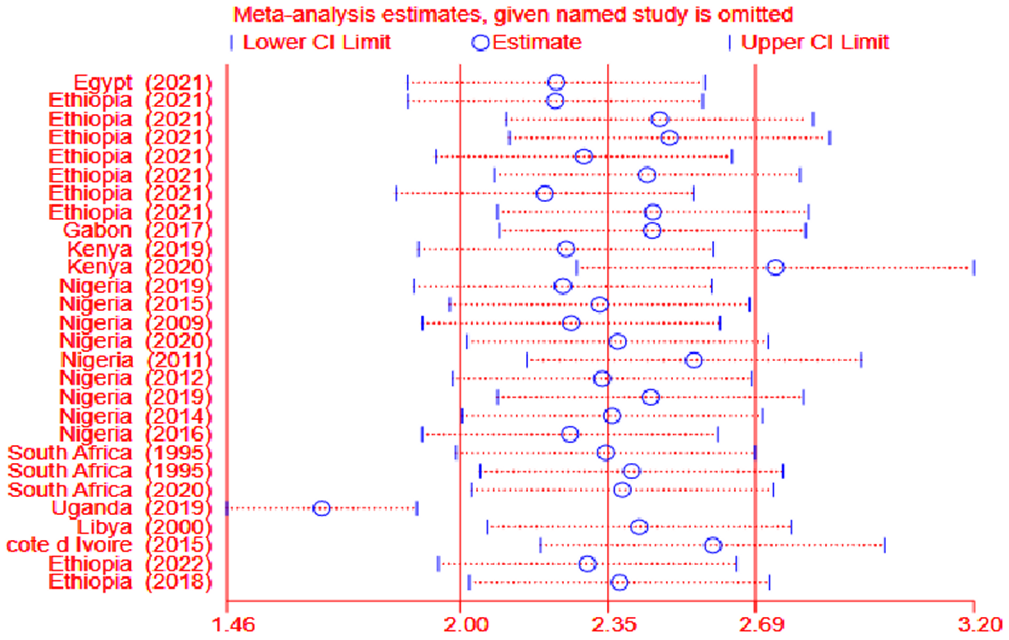

Figure 5 Sensitivity analysis to see the influence of each study in Africa.

peripheral neuropathy in mothers and abnormalities in fetuses have been linked to folate insufficiency (congenital abnormalities). It has long been known that adding folic acid to the diet around the time of conception lowers the likelihood that the child would have neural tube abnormalities. Thus, folic acid has a significant impact on the growth and development of the fetus during pregnancy.[63] Studies have shown that getting enough folic acid may reduce the risk of serious neural tube defects in the baby by at least 50%.[64]

As comparison to women without a history of medical issues, newborns born to those moms are 4.72 times more likely to suffer congenital abnormalities. Infants are more likely to have congenital anomalies, such as congenital heart problems, when their mothers have certain medical conditions or diseases. An investigation was carried out in Canada lends credence to this evidence.[65] To lower the risk of congenital defects in their unborn children, pregnant mothers must receive the right medical treatment in order to monitor and manage any medical disorders or illnesses.

Neonates born from mothers who had history drug use are 2.74 times high likely to suffer congenital anomalies when compared with their counterparts. Studies have shown that using drugs or pharmaceuticals excessively while pregnant can harm the baby and newborn. Congenital abnormalities in neonates can be a result of medication use during pregnancy.[66] Birth defects are more likely to occur when taking certain medications, such as teratogenic ones.[67] Concerns concerning possible pharmacological side effects, such as the chance of congenital birth abnormalities, may also exist in pregnant women. To reduce the possibility of adverse effects on the fetus, pregnant women should always check with their healthcare professional before taking any drugs.

In the present review, advanced maternal age (>35 years) has significant association with congenital anomalies when compared with mothers less than 35 years old. It increases the risk of congenital anomalies in the fetus by 1.97-fold. Advanced maternal age increases the risk of chromosomal abnormalities in newborns, such as Down syndrome.[68] As women age increases, the likelihood of errors in chromosomal division increases. In particular, the risk of non-disjunction, the failure of chromosomes to separate properly during meiosis, increases with advancing maternal age. This can lead to the formation of gametes with an abnormal number of chromosomes, which may result in chromosomal abnormalities in the offspring.[68] It is important for women of advanced maternal age to receive proper prenatal care and genetic counselling to manage the risk of congenital anomalies in their newborns.

The odds of congenital anomalies among mothers who drunk alcohol is 3.34 times higher compared with mothers without drinking alcohol. This finding is in agreement with clinical evidence that alcohol consumption during pregnancy can cause congenital anomalies in the developing fetus. The mechanism behind this is not entirely clear, but it is thought to be due to the toxic effects of alcohol on fetal development. The developing fetus is unable to metabolise alcohol as efficiently as an adult, leading to higher levels of alcohol in the fetal bloodstream and tissues. This can result in damage to developing organs, including the brain, and disrupt the normal processes of fetal development. Alcohol consumption during pregnancy has been linked to fetal alcohol spectrum disorders, which can cause physical, behavioural and cognitive abnormalities in affected individuals.[69] It is important for pregnant women to avoid alcohol consumption to prevent the risk of congenital anomalies in their developing fetus.

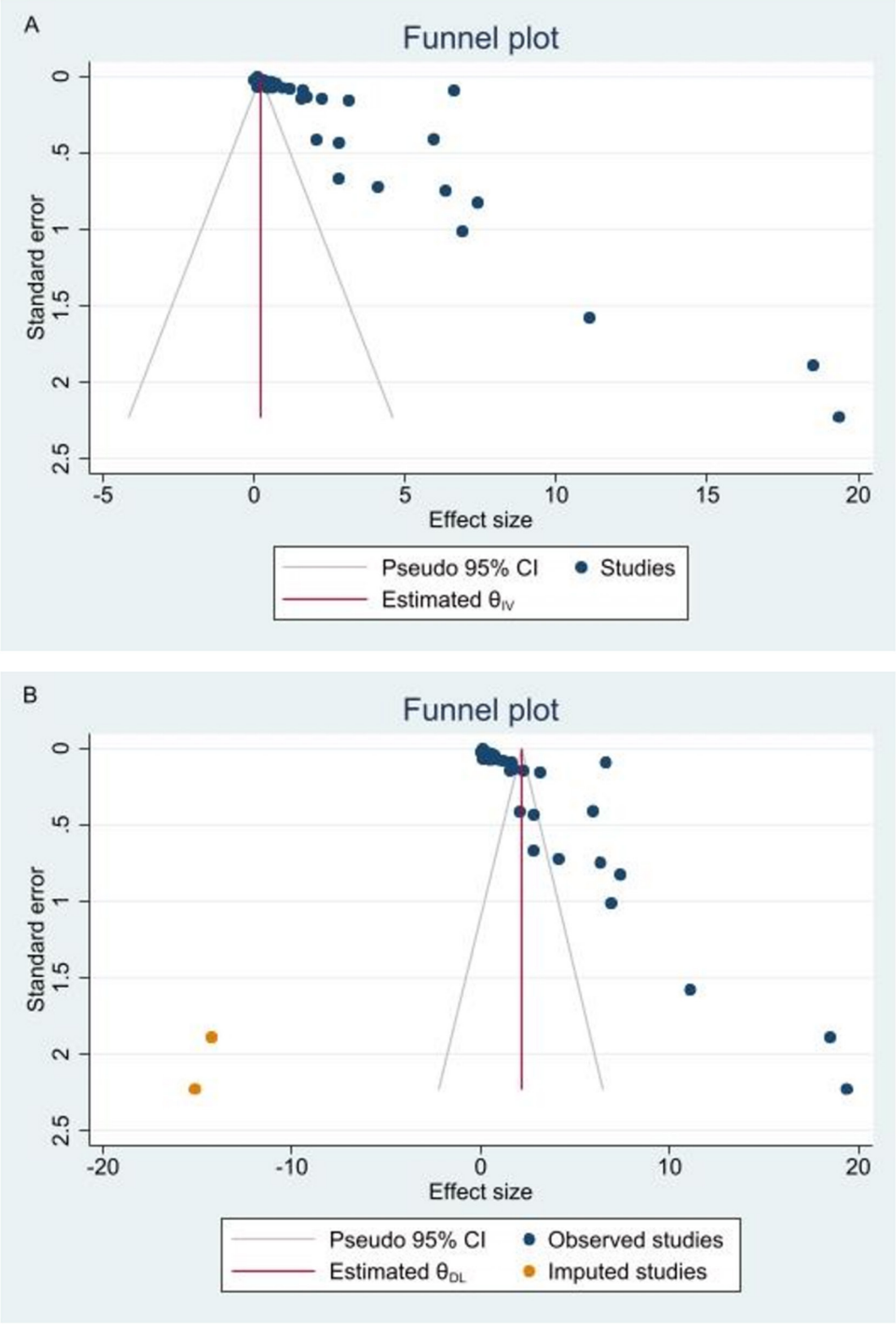

Figure 6 (A) A funnel plot with a pseudo 95% confidence limits used to test for publication bias. (B) A funnel plot with a pseudo 95% confidence limit after a trim-and-fill analysis two studies have a been imputed.

Infants born from mother who had experienced kchat chewing is 3.34 times high likely to have birth defects when compared with their counter parts. The mechanisms of khat chewing during pregnancy causing congenital anomalies are not well established. However, khat contains several psychoactive substances, including cathinone and cathine, which have been shown to cross the placental barrier and affect fetal development.[70 71] Cathinone and cathine act as sympathomimetic agents, increasing heart rate, blood pressure and causing

Table 4 Summary of articles included in meta-analysis for association with congenital anomalies 2023

Associated factors	OR (95% CI)	I^2(%)	First author	Year	Country
Folic acid supplementation	2.76 (1.32 to 5.76)		Birhanu *et al*[11]	2021	Ethiopia
	17.64 (6.51 to 47.8)		Gedamu *et al*[40]	2021	Ethiopia
	1.8 (1.14 to 2.85)		Jemal *et al*[43]	2021	Ethiopia
	7.2 (4.36 to 11.91)		Tsehay *et al*[57]	2019	Ethiopia
	1.76 (1.32 to 2.35)		Abebe *et al*[32]	2021	Ethiopia
	4.05 (0.96 to 17.13)		Getachew *et al*[42]	2023	Ethiopia
	5.38 (3.24 to 8.95)		Adane *et al*[54]	2018	Ethiopia
	0.54 (0.16 to 1.83)		Ajao *et al*[34]	2019	Nigeria
	0.56 (0.32 to 0.97)		Kishimba *et al*[44]	2015	Tanzania
Pooled OR	2.67 (1.42 to 5.00)	90.32			
Smoking	2.18 (0.5 to 9.46)		Gedamu *et al*[40]	2021	Ethiopia
	0.16 (0.1 to 0.26)		Jemal *et al*[43]	2021	Ethiopia
	3.85 (1.88 to 7.88)		Abebe *et al*[32]	2021	Ethiopia
Pooled OR	1.07 (0.1 to 11.68)	96.48			
Maternal illness	0.43 (0.13 to 1.44)		Birhanu *et al*[11]	2021	Ethiopia
	8.19 (2.68 to 25.00)		Gedamu *et al*[40]	2021	Ethiopia
	2.50 (1.55 to 4.04)		Jemal *et al*[43]	2021	Ethiopia
	1.13 (0.78 to 1.64)		Mekonen *et al*[46]	2021	Ethiopia
	1.12 (0.78 to 1.63)		Abebe *et al*[32]	2021	Ethiopia
	8.43 (5.19 to 13.68)		Getachew *et al*[42]	2023	Ethiopia
	4.72 (2.85 to 7.82)		Seyoum[54]	2018	Ethiopia
Pooled OR	2.44 (1.2 to 4.94)	92.10			
Unidentified drug use	3.80 (2.36 to 6.12)		Jemal *et al*[43]	2021	Ethiopia
	0.95 (0.75 to 1.20)		Mekonen *et al*[46]	2021	Ethiopia
	1.30 (0.80 to 2.11)		Abebe *et al*[32]	2021	Ethiopia
	3.02 (0.64 to 14.29)		Ajao *et al*[34]	2019	Nigeria
	10.32 (4.84 to 22.00)		Getachew *et al*[42]	2023	Ethiopia
	3.66 (2.22 to 6.03)		Seyoum[54]	2018	Ethiopia
Pooled OR	2.74 (1.29 to 5.81)	92.51			
Maternal age	16.28 (7.04 to 37.66)		Gedamu *et al*[40]	2021	Ethiopia
	2.91 (2.08 to 4.07)		Mekonen *et al*[46]	2021	Ethiopia
	0.83 (0.56 to 1.22)		Mekonnen *et al*[47]	2020	Ethiopia
	5 (2.15 to 11.63)		Tsehay *et al*[57]	2019	Ethiopia
	1.4 (0.43 to 4.59)		Mombo *et al*[49]	2017	Gabon
	1.52 (0.52 to 4.43)		Ajao *et al*[34]	2019	Nigeria
	1.04 (0.96 to 1.12)		Anyanwu *et al*[35]	2015	Nigeria
	1.07 (0.42 to 2.73)		Kishimba *et al*[44]	2015	Tanzania
	1.06 (0.36 to 3.14)		Getachew *et al*[42]	2023	Ethiopia
Pooled OR	1.97 (1.15 to 3.37)	91.00			
Ante natal care	2.51 (1.55 to 4.06)		Elawady *et al*[12]	2021	Egypt
	7.9 (3.44 to 18.17)		Gedamu *et al*[40]	2021	Ethiopia
	0.91 (0.71 to 1.16)		Mekonen *et al*[46]	2021	Ethiopia
	0.24 (0.15 to 0.4)		Mekonnen *et al*[47]	2020	Ethiopia
	0.78 (0.3 to 2.01)		Ajao *et al*[34]	2019	Nigeria
Pooled OR	1.25 (0.48 to 3.22)	94.28			

Continued

Table 4 Continued

Associated factors	OR (95% CI)	I^2(%)	First author	Year	Country
Alcohol	1.51 (0.2 to 11.4)		Gedamu *et al*[40]	2021	Ethiopia
	7.92 (4.87 to 12.88)		Jemal *et al*[43]	2021	Ethiopia
	2.67 (0.98 to 7.28)		Mekonnen *et al*[47]	2020	Ethiopia
	9.4 (4.41 to 20.04)		Tsehay *et al*[57]	2019	Ethiopia
	1.28 (0.51 to 3.22)		Getachew *et al*[42]	2023	Ethiopia
	1.58 (0.98 to 2.54)		Seyoum[54]	2018	Ethiopia
Pooled OR	3.15 (1.4 to 7.04)	85.16			
Kchat chewing	7.92 (4.85 to 12.93)		Jemal *et al*[43]	2021	Ethiopia
	2.69 (1.71 to 4.24)		Mekonnen *et al*[47]	2020	Ethiopia
	1.56 (0.79 to 3.08)		Abebe *et al*[32]	2021	Ethiopia
	3.49 (1.69 to 7.21)		Getachew *et al*[42]	2023	Ethiopia
Pooled OR	3.34 (1.68 to 6.65)	82.68			
Residence	0.48 (0.26 to 0.89)		Elawady *et al*[12]	2021	Egypt
	0.51 (0.29 to 0.88)		Birhanu *et al*[11]	2021	Ethiopia
	0.24 (0.1 to 0.59)		Gedamu *et al*[40]	2021	Ethiopia
	0.69 (0.38 to 1.26)		Mekonnen *et al*[47]	2020	Ethiopia
	0.47 (0.29 to 0.76)		Mekonnen *et al*[48]	2021	Ethiopia
	1.51 (0.96 to 2.38)		Tsehay *et al*[57]	2019	Ethiopia
Pooled OR	0.58 (0.36 to 0.95)	76.73			

vasoconstriction. These effects can reduce blood flow to the developing fetus, potentially leading to fetal growth restriction and other adverse outcomes.[70] Additionally, khat chewing has been linked to preterm labour and low birth weight in pregnant women. It is important for pregnant women to avoid khat chewing to prevent the risk of congenital anomalies in their developing fetus.

When compared with mothers who live in urban areas, the likelihood of congenital abnormalities is reduced by 42% in rural areas. This result is consistent with the research done in Ethiopia.[48 57] and China.[72] This may be a result of Ethiopia's rural communities' varied dietary practices and non-fat diet[73] and environmental factors such as air pollution, radiation, exposure to chemicals and/or to pesticides.[74] On the other hand, this finding is contradicted with the studies conducted in Egypt.[12]

The results of this review will aid in strengthening the prevention and control initiatives in African nations. In order to prioritise interventions in Africa, clinical and policy guidelines may need to be modified in light of the severity of birth abnormalities and the documented variations in prevalence estimates between nations. It would be extraordinary if the next step was for all African nations to enact laws requiring the fortification of food with folic acid. In addition, each nation should establish or enhance reliable surveillance systems to monitor all pregnancy-related outcomes, notably birth abnormalities. Significantly, this analysis emphasises the prevalence of congenital defects among newborns in African nations, giving crucial proof for decision-makers, medical professionals and other interested parties who have downplayed the severity of this problem.

Despite the review's many advantages, several limitations should be taken into consideration when interpreting its results. For example, the prevalence estimates may be lower because terminations of pregnancies and cases of congenital defects were not included in the estimate. Moreover, the variance in sample sizes between the included studies may have an impact on the pooled prevalence estimates. Also, the fact that there is a lot of diversity between nations may understate Africa's overall load. Due to the scarcity of information on congenital malformations, the evaluation included research from ten African nations.

In conclusion, it was discovered that Africa has a significant rate of congenital abnormalities. Congenital abnormalities were found to be prevalently prevalent in Kenya, Egypt, Uganda, Nigeria and Ethiopia. Congenital abnormalities were significantly associated with not taking folic acid supplements, a history of maternal sickness, a history of drug use, maternal age (>35 years), drinking alcohol, chewing khat and living in an urban area. The prevalence of congenital abnormalities among newborns in Africa can be decreased through proper folate supplementation during pregnancy, proper management of maternal illness, proper antenatal care, referral to medical personnel before using drugs, abstinence from alcohol consumption and kchat chewing. Also, we want to alert decision-makers to set robust prevention and control measures by prioritising them. Also, due to the scarcity

of data on congenital malformations, more primary and extensive study is required to better understand the true scale of the disorders and support preventive measures for preventable factors in Africa.

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Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests No, there are no competing interests.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request.

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73 Bentham J, Michell AC, Lockstone H, *et al*. Maternal high-fat diet interacts with embryonic Cited2 genotype to reduce Pitx2C expression and enhance Penetrance of left–right Patterning defects. *Hum Mol Genet* 2010;19:3394–401.
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PubMed Searching Methods

S.no.	Searching terms	Number of articles
1.	("Prevalence"[Mesh] OR Prevalence OR magnitude)	1,425,841
2.	("Congenital Abnormalities"[Mesh] OR "Congenital anomalies" OR "birth defects")	132,900
3.	("Infant, Newborn"[Mesh] OR neonates OR newborns)	246,364
4.	((((("Prevalence"[Mesh] OR Prevalence OR magnitude) AND (ffrft[Filter])) AND (("Congenital Abnormalities"[Mesh] OR "Congenital anomalies" OR "birth defects") AND (ffrft[Filter]))) AND (("Infant, Newborn"[Mesh] OR neonates OR newborns) AND (ffrft[Filter]))) AND (Africa AND (ffrft[Filter])) AND (ffrft[Filter])	289

JBI Critical Appraisal Checklist

JBI Critical Appraisal Checklist for Studies Reporting Prevalence Data

Reviewer _____ Date _____

Author _____ Year _____ Record Number _____

	Yes	No	Unclear	Not applicable
1. Was the sample frame appropriate to address the target population?	☐	☐	☐	☐
2. Were study participants sampled in an appropriate way?	☐	☐	☐	☐
3. Was the sample size adequate?	☐	☐	☐	☐
4. Were the study subjects and the setting described in detail?	☐	☐	☐	☐
5. Was the data analysis conducted with sufficient coverage of the identified sample?	☐	☐	☐	☐
6. Were valid methods used for the identification of the condition?	☐	☐	☐	☐
7. Was the condition measured in a standard, reliable way	☐	☐	☐	☐

for all participants?

8. Was there appropriate statistical analysis? ☐ ☐ ☐ ☐

9. Was the response rate adequate, and if not, was the low ☐ ☐ ☐ ☐

response rate managed appropriately?

Overall appraisal: Include ☐ **Exclude** ☐ **Seek further info** ☐

Comments (Including reason for exclusion)

_____

_____

_____

JBI Critical Appraisal Checklist for Analytical Cross Sectional Studies

Reviewer _____ Date _____

Author _____ Year _____ Record Number _____

	Yes	No	Unclear	Not applicable
1. Were the criteria for inclusion in the sample clearly defined?	☐	☐	☐	☐
2. Were the study subjects and the setting described in detail?	☐	☐	☐	☐
3. Was the exposure measured in a valid and reliable way?	☐	☐	☐	☐
4. Were objective, standard criteria used for measurement of the condition?	☐	☐	☐	☐
5. Were confounding factors identified?	☐	☐	☐	☐
6. Were strategies to deal with confounding factors stated?	☐	☐	☐	☐
7. Were the outcomes measured in a valid and reliable way?	☐	☐	☐	☐

8. Was appropriate statistical analysis used? ☐ ☐ ☐ ☐

Overall appraisal: Include ☐ **Exclude** ☐ **Seek further info** ☐

Comments (Including reason for exclusion)

_____

_____

_____

JBI Critical Appraisal Checklist for Case Control Studies

Reviewer _____ Date _____

Author _____ Year _____ Record Number _____

		Yes	No	Unclear	Not applicable
1.	Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?	☐	☐	☐	☐
2.	Were cases and controls matched appropriately?	☐	☐	☐	☐
3.	Were the same criteria used for identification of cases and controls?	☐	☐	☐	☐
4.	Was exposure measured in a standard, valid and reliable way?	☐	☐	☐	☐
5.	Was exposure measured in the same way for cases and controls?	☐	☐	☐	☐

of the identified sample?

6. Were confounding factors identified? ☐ ☐ ☐ ☐

7. Were strategies to deal with confounding factors stated? ☐ ☐ ☐ ☐

8. Were outcomes assessed in a standard, valid and reliable way for cases and controls? ☐ ☐ ☐ ☐

9. Was the exposure period of interest long enough to be meaningful? ☐ ☐ ☐ ☐

10. Was appropriate statistical analysis used? ☐ ☐ ☐ ☐

Overall appraisal: Include ☐ **Exclude** ☐ **Seek further info** ☐

Comments (Including reason for exclusion)

_____

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_____

JBI Critical Appraisal Checklist for Cohort Studies

Reviewer _____ Date _____

Author _____ Year _____ Record Number _____

	Yes	No	Unclear	Not applicable
1. Were the two groups similar and recruited from the same population?	☐	☐	☐	☐
2. Were the exposures measured similarly to assign people to both exposed and unexposed groups?	☐	☐	☐	☐
3. Was the exposure measured in a valid and reliable way?	☐	☐	☐	☐
4. Were confounding factors identified?	☐	☐	☐	☐
5. Were strategies to deal with confounding factors stated?	☐	☐	☐	☐
6. Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	☐	☐	☐	☐
7. Were the outcomes measured in a valid and reliable way?	☐	☐	☐	☐

8. Was the follow up time reported and sufficient to be long enough for outcomes to occur? ☐ ☐ ☐ ☐
9. Was follow up complete, and if not, were the reasons to loss to follow up described and explored? ☐ ☐ ☐ ☐
10. Were strategies to address incomplete follow up utilized? ☐ ☐ ☐ ☐
11. Was appropriate statistical analysis used? ☐ ☐ ☐ ☐

Overall appraisal: Include ☐ **Exclude** ☐ **Seek further info** ☐

Comments (Including reason for exclusion)

_____

_____

_____

Supplementary file 4: (A) The quality status of studies based on JBI critical appraisal checklist for studies reporting prevalence data

Studies	Appropriate sampling frame?	Appropriate sampling?	Adequate sample size?	Detail setting description?	Analysis with sufficient coverage?	Valid method to identify the condition?	Reliable measurement?	Appropriate statistical analysis?	Adequate response rate?	Total, out of 9
Kouame et al	Yes	N/A	yes	yes	Yes	Yes	UC	Yes	N/A	7
Elawady et al	Yes	Yes	Yes	Yes	Yes	UC	UC	Yes	UC	6
Birhanu et al	Yes	Yes	Yes	Yes	Yes	UC	UC	Yes	UC	4
Gedamu et al	Yes	N/A	Yes	Yes	Yes	Yes	UC	Yes	N/A	8
Geneti et al	Yes	N/A	Yes	Yes	Yes	Yes	Yes	Yes	N/A	9
Mekonen et al	Yes	N/A	Yes	Yes	Yes	Yes	UC	Yes	N/A	8
Mekonnen et al	Yes	N/A	Yes	Yes	Yes	Yes	Uc	Yes	N/A	8
Sileshi et al	Yes	N/A	Yes	Yes	Yes	Yes	Yes	Yes	N/A	9
Getachew et al	Yes	N/A	Yes	Yes	Yes	Yes	UC	Yes	N/A	8
Adane et al	Yes	N/A	Yes	No	Yes	Yes	No	Yes	N/A	7
Mombo et al	Yes	N/A	Yes	No	Yes	UC	No	Yes	N/A	6
Wgathu et al	Yes	Yes	Yes	Yes	Yes	Yes	UC	UC	UC	4
Agot et al	Yes	N/A	Yes	Yes	Yes	Yes	UC	Yes	N/A	8
Singh et al	Yes	N/A	Yes	Yes	No	UC	Yes	Yes	N/A	7
Ajao et al	Yes	N/A	Yes	Yes	Yes	Yes	Yes	Yes	N/A	9
Anyanwu et al	Yes	N/A	Yes	No	Yes	Yes	UC	Yes	N/A	7
Bakare et al	Yes	N/A	Yes	No	Yes	Yes	UC	Yes	N/A	7
Chukwubuike et al	Yes	N/A	Yes	Yes	Yes	Yes	Yes	Yes	N/A	9
Ekanem et al	Yes	N/A	Yes	No	Yes	UC	UC	Yes	N/A	6
Obu et al	Yes	N/A	Yes	Yes	Yes	Yes	Yes	Yes	N/A	9
Oluwafemi et al	Yes	N/A	Yes	Yes	Yes	Yes	UC	Yes	N/A	8
Onankpa et al	Yes	N/A	Yes	Yes	Yes	UC	UC	Yes	N/A	7
MAN et al	Yes	N/A	Yes	Yes	Yes	Yes	UC	Yes	N/A	8
Venter et al	Yes	N/A	Yes	Yes	Yes	Yes	UC	Yes	N/A	8
Delport et al	Yes	N/A	Yes	Yes	Yes	Yes	Yes	Yes	N/A	9
Saib et al	Yes	N/A	Yes	Yes	Yes	Yes	Yes	Yes	N/A	9
Wwanja et al	Yes	N/A	Yes	Yes	Yes	Yes	Yes	UC	N/A	8

Supplementary file 4: (B) The quality status of studies based on JBI critical appraisal checklist for studies reporting case control studies.

Studies	Were the group comparable?	Were cases and controls matched?	Were the same criteria for identification	Was exposure measured in a standard, valid and reliable way?	Was exposure measured in the same way ?	Were confounding factors identified?	Were strategies to deal the confounders stated?	Were outcomes assessed in a standard, valid and reliable way?	Was the exposure period of interest long enough	Was appropriate statistical analysis used?	Total out of 10
Jemal et al	Yes	No	Yes	UC	Yes	Yes	Yes	Yes	UC	Yes	7
Mekonnen et al	Yes	No	Yes	UC	Yes	Yes	Yes	Yes	UC	Yes	7
Tsehay et al	Yes	NO	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	8
Abebe et al	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	UC	Yes	8
Kishimba et al	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9