Prevalence of perinatal anxiety in low- and middle-income countries: A systematic review and meta-analysis

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ABSTRACT

Background: Perinatal anxiety is associated with adverse outcomes for women and their infants. Women in low- and middle-income countries (LMIC) may be at higher risk of perinatal anxiety. We aimed to systematically review and synthesise the evidence on prevalence of perinatal anxiety in LMIC.

Method: We searched MEDLINE, Embase, PscyhINFO, Global Health and Web of Science to identify studies assessing prevalence of perinatal anxiety in LMIC. Studies published since January 2016 were included. Screening and data extraction was conducted independently by two reviewers. Pooled prevalence estimates were calculated using random-effect meta-analyses and sources of heterogeneity explored through subgroup analyses and meta-regression.

Results: We screened 9494 titles and abstracts, reviewed 700 full-texts and included 54 studies in the systematic review and meta-analysis. The pooled prevalence of self-reported anxiety symptoms was 29.2% (95%CI 24.5–34.2; I^2 98.7%; 36 studies; n = 28,755) antenatally and 24.4% (95%CI 16.2–33.7; I^2 98.5%; 15 studies; n = 6370) postnatally. The prevalence of clinically-diagnosed anxiety disorder was 8.1% (95%CI 4.4–12.8; I^2 88.1% 5 studies; n = 1659) antenatally and 16.0% (95% CI 13.5–18.9; n = 113) postnatally.

Limitations: Our search was limited to studies published since January 2016 in order to update a previous review on this topic.

Conclusion: Perinatal anxiety represents a significant burden in LMIC, with one in four women experiencing symptoms during pregnancy or postpartum. Research remains lacking in a significant proportion of LMIC, particularly in the lowest income countries. Further research should guide application of screening tools in clinical settings to identify women with anxiety disorders in order to provide appropriate treatment.

1. Introduction

Mental disorders are one of the commonest morbidities of the perinatal period (Howard et al., 2014). Anxiety experienced during pregnancy and postnatally is associated with a range of adverse outcomes for women and their infants (Stein et al., 2014; Grigoriadis et al., 2019). Women with perinatal anxiety are more likely to experience poorer coping strategies, fear of childbirth, postnatal depression and suicide while their infants are at higher risk of pre-term birth and poor cognitive, emotional and behavioral development (Grigoriadis et al., 2019; Rubertsson et al., 2014; Coelho et al., 2011; Ding et al., 2014; Glasheen et al., 2010). The estimated prevalence of perinatal anxiety disorders varies according to cultural context, participant characteristics, timing during the perinatal period as well as methodological factors such as whether self-report instruments or diagnostic interviews are used. A meta-analysis by Dennis et al. (2017) reported a pooled prevalence of clinically diagnosed anxiety disorder of 15.2% antenatally and 9.9% postnatally, while a meta-analysis by Fawcett et al. (2019) reported a pooled prevalence of 20.7% across the perinatal period (Dennis et al., 2017; Fawcett et al., 2019). These pooled estimates are heavily dominated by studies from high-income countries (HIC). In Dennis et al.'s (2017) review, for instance, only 13 of the 102 included studies

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contributing to the meta-analyses were conducted in low- and middle-income countries (LMIC).

Women in LMIC are likely to be at higher risk of mental disorders due to greater exposure to stressors and risks factors. These include a greater likelihood of socio-economic deprivation, more severe and more chronic poverty, higher co-morbidity with chronic medical conditions, socio-cultural factors such as gender inequity and poorer levels of education among women and persisting stigma around mental health disorders (Howard et al., 2014; Gelaye et al., 2016; Norhayati et al., 2015; Fisher et al., 2012). Additionally, the identification and treatment of mental disorders in many LMIC is more limited due to a scarcity of mental health services (Fisher et al., 2012). Dennis et al. conducted a subgroup analysis by countries' income groups and identified a prevalence of perinatal anxiety symptoms of 34.4% in LMIC compared with 19.4% in HIC (Dennis et al., 2017). Reliable prevalence estimates from LMIC are crucial to understanding the burden of anxiety disorders in these settings and highlighting the need for clinical attention. We aim to systematically review and synthesise the evidence on the prevalence of anxiety among pregnant and postpartum women in LMIC. This is the first review to focus specifically on LMIC settings. Our review incorporates the large body of evidence that has emerged in this field in recent years and therefore updates two previous global reviews on this topic (Dennis et al., 2017; Fawcett et al., 2019).

2. Methods

2.1. Search strategy and study eligibility

The protocol and results of this systematic review are reported according to PRISMA guidelines (Moher et al., 2009) (SI1). We searched MEDLINE, Embase, PsychINFO, Global Health, Web of Science, *Google* and *Google Scholar* using a combination of keywords and MeSH search terms pertaining to perinatal status, anxiety disorders and LMIC adapted to each database (SI2). We limited the search to studies published since 1 January 2016: this date was selected to identify studies published since the last comprehensive reviews on this topic which included studies up to January 2016 and July 2016 (Dennis et al., 2017; Fawcett et al., 2019). Reference lists of relevant publications were hand-searched for further relevant articles. Studies were included if they were cross-sectional or cohort studies; included women who were pregnant or up to twelve months post-partum; assessed prevalence of anxiety symptoms or anxiety disorders; used a diagnostic interview or validated screening instrument; and were conducted in LMIC as defined using World Bank country classifications. Our PICOS approach is summarised in SI3. We excluded studies of pregnancy- or labour-specific anxiety; validation, case-control and intervention studies; studies of high-risk women (e.g. women with birth trauma); and studies reporting anxiety prevalence in combination with other disorders (e.g. prevalence of common mental disorders). Our protocol was registered on PROSPERO (CRD42020218815) on 16 November 2020. The final search was carried out on 4 November 2020.

2.2. Screening, data extraction and quality assessment

Two authors (MNS, GF) independently screened titles and abstracts of all identified references and full-texts of potentially relevant articles. Any discrepancies were resolved through discussion with a third author (FA). Two authors (MNS, GF) independently extracted data from included studies on study design, location, participant characteristics, recruitment method, perinatal status, assessment instrument and cut-offs. Prevalence was extracted in the form of number of cases and total participants. If studies reported only mean data, did not report a cut-off point for anxiety or had other missing data, we contacted authors for additional information. Study quality was assessed independently by two authors (MNS, GF) using an adapted version of the Effective Public Health Practice Project Quality Assessment Tool for Observational Studies (Armijo-Olivo et al., 2012). Studies were scored as being at high, moderate or low risk of selection, detection and attrition bias. Selection bias was assessed by representativeness of the study population and response rate; detection bias was assessed according to outcome assessment (clinical interview vs. self-report); and attrition bias was assessed by participation rate and missing data (SI4). Any discrepancies in risk of bias assessments were discussed with a third author (FA).

2.3. Data synthesis and analysis

Following a narrative synthesis of included studies, we conducted meta-analysis using the cases and denominator from each study to calculate pooled prevalence estimates with 95% confidence intervals (CI) for antenatal and postnatal anxiety. We also calculated 95% prediction intervals (PI) to illustrate which range of true prevalence rates might be expected across different settings (IntHout et al., 2016). We used the double-arcsine method to transform prevalence estimates in order to avoid the weight of studies with prevalence nearing either 0% or 100% being over-estimated; pooled estimates were back-transformed to ease interpretation (Barendregt et al., 2013). We used a DerSimonian and Laird random-effects model based on our assumption that prevalence estimates across studies would differ but follow a normal distribution; although we expected a high degree of heterogeneity a-priori, we believed that prevalence across settings would nevertheless stem from a single normal distribution of prevalence which could be pooled. When more than one publication used the same data only one study was included in meta-analysis: the study which was included was selected on the basis of the following criteria (in order of importance): (i) use of diagnostic interview (rather than self-report); (ii) sample size. When studies assessed prevalence in the same participants at multiple time-points, we avoided double-counting participants in meta-analyses by limiting data to one timepoint per meta-analysis group. Statistical heterogeneity was assessed using the I^2 statistic with values >75% indicating significant heterogeneity (Higgins and Thompson, 2002). Potential causes of heterogeneity were explored through subgroup analyses and meta-regression which were planned a-priori according to assessment method (clinical interview vs. screening instrument); geographical location; type of anxiety (generalized anxiety disorder (GAD), state anxiety, any anxiety); and study quality (high, moderate or low risk of selection, detection and attrition bias). Random-effects meta-regression models including each of these covariates separately were run to further explore heterogeneity. As sensitivity analyses we ran meta-analyses and meta-regression using fixed-effects, results of which are presented in supplementary tables. The presence of publication bias was explored assessing the symmetry of the distribution of standardised prevalence estimates across studies, with asymmetry in this distribution interpreted as evidence of publication bias (Lin and Chu, 2018; Furuya-Kanamori et al., 2018; Hunter et al., 2014). All analyses were conducted in Stata version 14.2.

3. Results

The literature search identified 12,796 records of which 3302 were duplicates (Fig. 1). We screened 9494 titles and abstracts and 700 full-texts. Ten additional records were identified through grey literature searches. We contacted 64 authors for additional information of whom seven replied and provided the data required for inclusion in our review. A total of 54 studies published in 56 publications were included in the systematic review and 54 studies were included in meta-analysis (Agbaje et al., 2019; Alipour et al., 2018; Aryal et al., 2018; Barthel et al., 2016; Bhushan et al., 2020; Boggaram et al., 2017; Çankaya, 2020; Castro e Couto et al., 2016; de Mello et al., 2021; Dikmen-Yildiz et al., 2017; Dönmez et al., 2016; Ezeme et al., 2018; Faramarzi et al., 2020; Ferraro et al., 2017; Gelaye et al., 2020; González-Mesa et al., 2019; Goyal et al., 2020; Gul et al., 2019; Hasanjanzadeh and Faramarzi, 2017; Jalal et al., 2017; Kang et al., 2016; Kariman et al., 2016; Koc et al.,
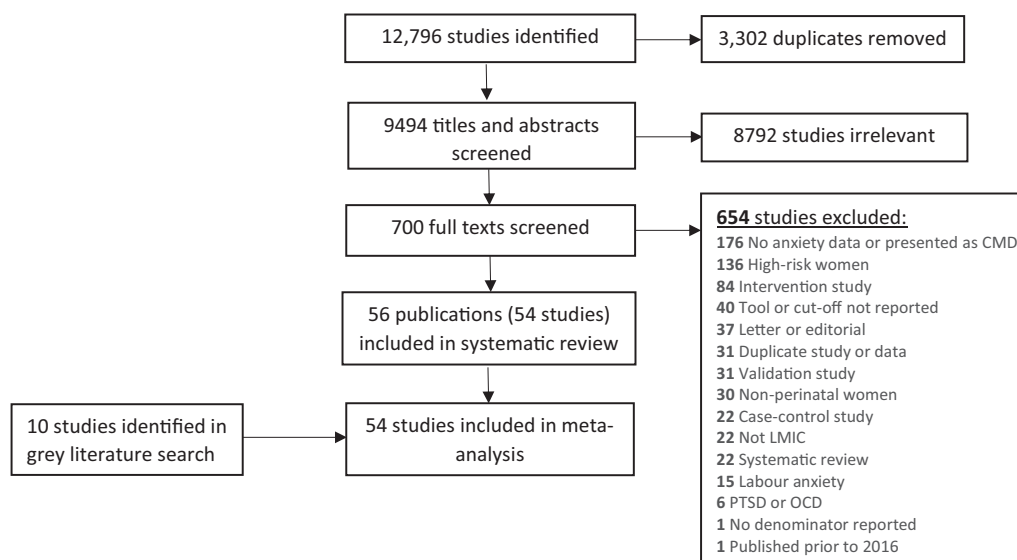
Fig. 1. Flow diagram of studies identified on the prevalence of perinatal anxiety.

2021; Li et al., 2019; Liu et al., 2020; Lu et al., 2020; Ma et al., 2019; Mahmoodi et al., 2017; Moameri et al., 2019; Morais, 2017; Nasreen et al., 2018; Nieto et al., 2019; Odinka et al., 2018; Osma-Zambrano et al., 2019; Petrovic et al., 2016; Priyambada et al., 2017; de Avila Quevedo et al., 2021; Rabia et al., 2017; Radeef et al., 2019; Redinger et al., 2018; Sahu, 2016; Sanchez et al., 2020; Shrestha and Pun, 2018; Silva et al., 2017; Tang et al., 2019; Türkmen et al., 2021; Umuziga et al., 2020; van Heyningen et al., 2017; Vidhya, 2017; Wang et al., 2021; Wassif et al., 2019; Yu et al., 2017; Yu et al., 2020a; Yu et al., 2020b; Zeng et al., 2017; Zhang et al., 2018). Reasons for exclusions are listed in Fig. 1. Two publications presented data from the *Pregnancy Outcomes, Maternal and Infant Cohort Study* (PROMIS) (Gelaye et al., 2020; Sanchez et al., 2020) and two publications presented data from the *Zhoushan Pregnant Women Cohort* (ZPWC) (Yu et al., 2017; Zhang et al., 2018). Of these, Gelaye et al., 2020 and Yu et al., 2017 were selected for inclusion in meta-analysis.

3.1. Study characteristics

Characteristics of included studies are summarised in SI5. Studies were conducted across eighteen countries. The countries with the greatest number of studies were China (n = 12), Iran (n = 7), Brazil (n = 6), India (n = 6) and Turkey (n = 6). Only one study was conducted in a low-income country (Rwanda); all other studies were conducted in lower-middle-income countries (n = 16) or upper-middle-income countries (n = 40). Eight studies used diagnostic interviews and 47 used screening tools (one study used both). The most commonly used diagnostic interviews were the Mini International Neuropsychiatric Interview (MINI; n = 6) and MINI-Plus (n = 2). The most commonly used screening tools were Zung's Self-rating Anxiety Scale (SAS; n = 10), the Hospital Anxiety and Depression Scale (HADS; n = 10), the State-Trait Anxiety Inventory (STAI; n = 6); the Generalized Anxiety Disorder Scale (GAD-7; n = 5); and the Depression, Anxiety and Stress Scale (DASS; n = 5). Anxiety prevalence ranged from 2.1% (van Heyningen et al., 2017) to 64% (Alipour et al., 2018) antenatally and from 0.4% (Radeef et al., 2019) to 67% (Türkmen et al., 2021) postnatally. Four studies reported anxiety prevalence across the combined antenatal and postnatal periods and reported perinatal prevalence estimates between 1.4% (Goyal et al., 2020) and 16.3% (Ferraro et al., 2017). Across all studies, the risk of selection bias was rated as high, moderate and low in 36, six and 14 studies, respectively. The risk of detection bias was rated as moderate in 48 and low in eight studies. The risk of attrition bias was

rated as high in four studies, moderate in three studies and low in 49 studies. Overall risk of bias scores are summarised in SI5; detailed scoring is summarised in SI6.

3.2. Prevalence of anxiety

The pooled prevalence of self-reported anxiety symptoms was 29.2% (95% CI 24.5–34.2; 95% PI 3.4–66.2; I^2 98.7%; 36 studies; n = 28,755) (Alipour et al., 2018; Aryal et al., 2018; Barthel et al., 2016; Bhushan et al., 2020; Çankaya, 2020; Dikmen-Yildiz et al., 2017; Dönmez et al., 2016; Ezeme et al., 2018; Faramarzi et al., 2020; Gelaye et al., 2020; González-Mesa et al., 2019; Gul et al., 2019; Hasanjanzadeh and Faramarzi, 2017; Kang et al., 2016; Li et al., 2019; Ma et al., 2019; Moameri et al., 2019; Morais, 2017; Nasreen et al., 2018; Nieto et al., 2019; Osma-Zambrano et al., 2019; Petrovic et al., 2016; Priyambada et al., 2017; Rabia et al., 2017; Radeef et al., 2019; Redinger et al., 2018; Sahu, 2016; Shrestha and Pun, 2018; Silva et al., 2017; Tang et al., 2019; Umuziga et al., 2020; Wang et al., 2021; Yu et al., 2017; Yu et al., 2020a; Yu et al., 2020b; Zeng et al., 2017) antenatally and 24.4% (95% CI 16.2–33.7; 95% PI 0.0–70.2; I^2 98.5%; 15 studies; n = 6370) (Agbaje et al., 2019; Aryal et al., 2018; Barthel et al., 2016; Dikmen-Yildiz et al., 2017; Jalal et al., 2017; Kariman et al., 2016; Liu et al., 2020; Mahmoodi et al., 2017; Nieto et al., 2019; Odinka et al., 2018; Radeef et al., 2019; Türkmen et al., 2021; Umuziga et al., 2020; Wassif et al., 2019; Zeng et al., 2017) postnatally (Table 1 and Fig. 2). The pooled prevalence of a clinically diagnosed anxiety disorder was 8.1% (95% CI 4.4–12.8; 95% PI 0.0–27.9; I^2 88.1%; 5 studies; n = 1659) (Boggaram et al., 2017; Castro e Couto et al., 2016; de Mello et al., 2021; van Heyningen et al., 2017; Vidhya, 2017) antenatally (SI7). Only one study assessed the postnatal clinically diagnosed anxiety disorder, reporting a prevalence of 16.0% (95% CI 13.5–18.9; n = 113) (de Avila Quevedo et al., 2021) postnatally. The prevalence of self-reported anxiety symptoms in the first, second and third trimesters was 25.7% (95% CI 16.4–36.3; I^2 99.4%; 95% PI 0.0–71.1; 14 studies; n = 15,307) (Alipour et al., 2018; Bhushan et al., 2020; Gelaye et al., 2020; González-Mesa et al., 2019; Gul et al., 2019; Li et al., 2019; Osma-Zambrano et al., 2019; Redinger et al., 2018; Shrestha and Pun, 2018; Silva et al., 2017; Tang et al., 2019; Wang et al., 2021; Yu et al., 2017; Yu et al., 2020a), 34.2% (95% CI 24.3–44.8; I^2 97.3%; 95% PI 5.0–72.7; 8 studies; n = 4362) (Alipour et al., 2018; Bhushan et al., 2020; Gul et al., 2019; Morais, 2017; Osma-Zambrano et al., 2019; Shrestha and Pun, 2018; Silva et al., 2017; Yu et al., 2017) and 28.5% (95% CI 22.6–34.7; 95% PI 5.6–59.9; I^2 97.8%;
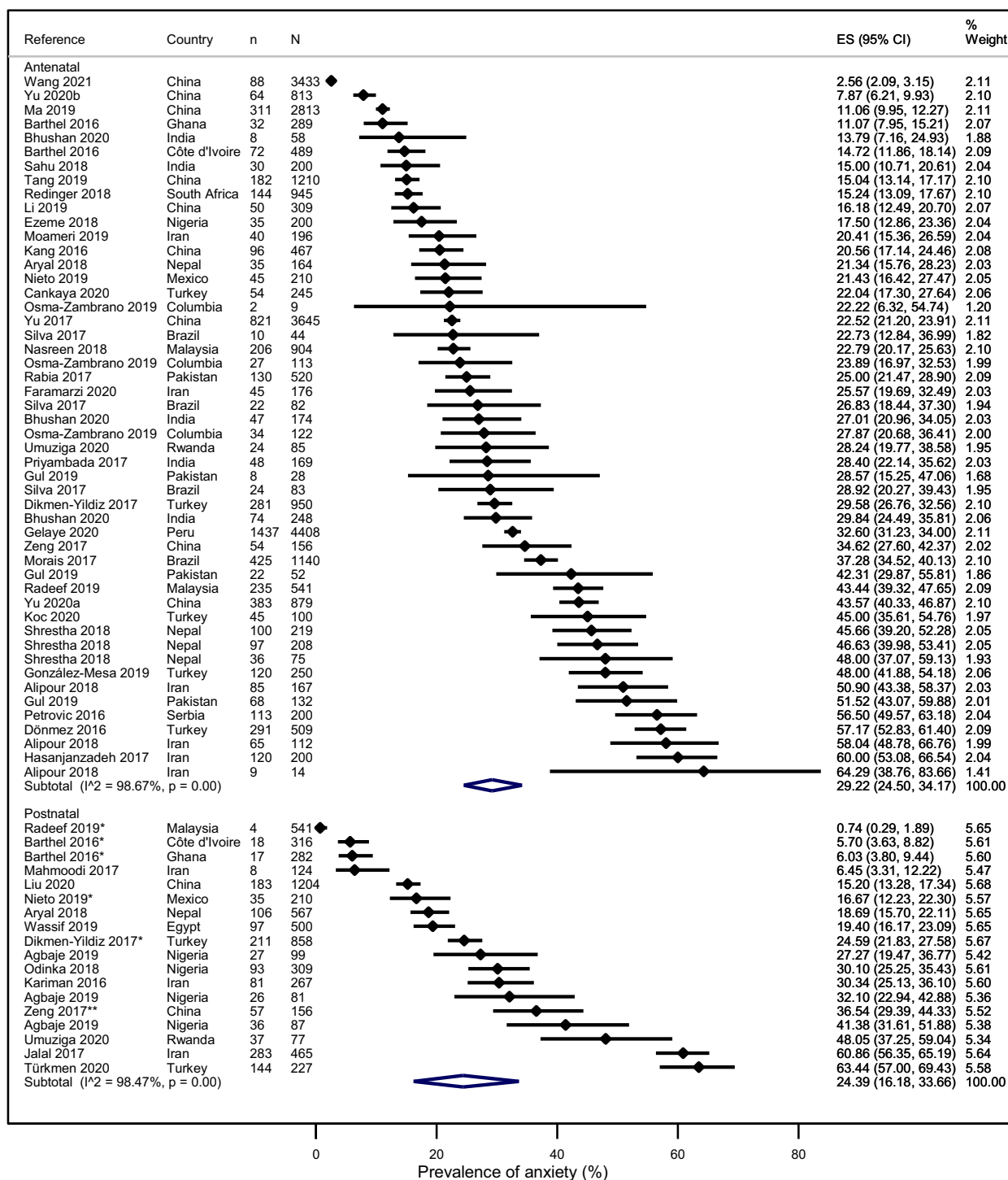
Fig. 2. Prevalence of antenatal and postnatal anxiety symptoms.
Abbreviations: n numerator; N denominator; ES effect size; CI confidence intervals.
Notes: Asterisks (*) indicate cohort studies; only one antenatal and one postnatal measure from these studies were included in this meta-analysis. All other studies are cross-sectional; those listed more than once reported results from different participants at different timepoints. Three studies which assessed prevalence of anxiety across the entire perinatal period combined are excluded.

19 studies; n = 11,114) (Alipour et al., 2018; Barthel et al., 2016; Bhushan et al., 2020; Çankaya, 2020; Dikmen-Yildiz et al., 2017; Gul et al., 2019; Kang et al., 2016; Koc et al., 2021; Ma et al., 2019; Nasreen et al., 2018; Nieto et al., 2019; Osma-Zambrano et al., 2019; Petrovic et al., 2016; Radeef et al., 2019; Shrestha and Pun, 2018; Silva et al., 2017; Yu et al., 2017; Yu et al., 2020b; Zeng et al., 2017), respectively. The prevalence of clinically diagnosed anxiety disorder in the first,

second and third trimesters was 9.84% (95% CI 7.0–13.6; 1 study; n = 315) (de Mello et al., 2021), 10.2% (95% CI 8.2–12.4; 2 studies; n = 808) (Castro e Couto et al., 2016; de Mello et al., 2021) and 7.5% (95% CI 4.2–11.6; 2 studies; n = 207) (Castro e Couto et al., 2016; Vidhya, 2017), respectively. When studies at high risk of selection or attrition bias were excluded from analyses, the pooled prevalence of self-reported anxiety symptoms was 30.7% (95% CI 24.8–36.9; 95% PI 8.4–59.1; I²

Table 1

Prevalence of self-reported anxiety symptoms and clinically-diagnosed anxiety disorder during the perinatal period.

Time period	All studies					Studies with low risk of selection and attrition bias				
	Studies	Sample	Pooled prevalence % (95% CI)	95% PI	I²%	Studies	Sample	Pooled prevalence % (95% CI)	95% PI	I²%
Antenatal										
First trimester										
Self-report	14	15,307	25.7 (16.4–36.3)	0.0–71.1	99.4	4	4494	32.8 (22.7–43.6)	2.1–75.4	61.2
Clinical diagnosis	*1*	*315*	*9.8 (7.0–13.6)*	–	–	*1*	*315*	*9.8 (7.0–13.6)*	–	–
Second trimester										
Self-report	8	4362	34.2 (24.3–44.8)	5.0–72.7	97.3	3	301	40.0 (25.3–55.8)	–	–
Clinical diagnosis	2	808	10.2 (8.2–12.4)	–	–	2	808	10.2 (8.2–12.4)	–	–
Third trimester										
Self-report	19	11,114	28.5 (22.6–34.7)	5.6–59.9	97.8	9	3605	29.4 (20.3–39.4)	3.0–67.7	97.3
Clinical diagnosis	2	207	7.5 (4.2–11.6)	–	–	*1*	*147*	*6.1 (3.3–11.2)*	–	–
All antenatal										
Self-report	36	28,755	29.2 (24.5–34.2)	3.4–66.2	98.7	14	8760	30.7 (24.8–36.9)	8.4–59.1	96.2
Clinical diagnosis	5	1659	8.1 (4.4–12.8)	0.0–27.9	88.1	2	1123	9.6 (7.1–12.4)	–	–
Postnatal										
Self-report	15	6370	24.4 (16.2–33.4)	0.0–70.2	98.5	7	2491	24.8 (19.2–30.9)	7.6–47.8	90.1
Clinical diagnosis	*1*	*706*	*16.0 (13.5–18.9)*	–	–	*1*	*706*	*16.0 (13.5–18.9)*	–	–

Abbreviations: *CI* confidence interval; *PI* prediction interval.
Notes: 95% PI and I² statistic inestimable with ≤3 studies. *Italics* indicate only one study in subgroup; these are not pooled estimates and are included for reference only.

96.2%; 14 studies; n = 8769) antenatally and 24.8% (95% CI 19.2–30.9; 95% PI 7.6–47.8; I² 90.1%; 7 studies; n = 2491) postnatally, and the pooled prevalence of clinically diagnosed anxiety disorders was 9.6% (95% CI 7.1–12.4; 2 studies; n = 1123) antenatally. Only one study assessed clinically diagnosed anxiety disorder postnatally and did not have a high risk of selection or attrition bias; this study reported a prevalence of 16.0% (95% CI 13.5–18.9; n = 706). A number of studies were significant outliers. Three Chinese studies reported estimates of antenatal anxiety symptoms which were significantly lower than the pooled estimate, with no overlap between their 95% CI and the 95% CI of the pooled estimate (Ma et al., 2019; Wang et al., 2021; Yu et al., 2020b), while two studies from Iran reported estimates of antenatal anxiety symptoms which were significantly higher than the pooled estimate (Fig. 2) (Alipour et al., 2018; Hasanjanzadeh and Faramarzi, 2017). Outliers for postnatal anxiety symptoms included estimates reported by Radeef et al. (2019) in Malaysia and Barthel et al. (2016) from Ghana and Côte d'Ivoire (Fig. 2) (Barthel et al., 2016; Radeef et al., 2019).

3.3. Subgroup analyses

Results of subgroup analyses are summarised in Table 2. The prevalence of self-reported anxiety symptoms varied by instrument used: antenatal prevalence was lowest using the GAD-7 (20.5%; 95% CI 9.5–34.5; 95% PI 0.0–78.8; I² 99.2%; 4 studies; n = 6878) and highest using the STAI (40.4%; 95% CI 17.1–66.3; 95% PI 0.0–100.0; I² 99.1%; 4 studies; n = 1804). Postnatal prevalence was lowest using the SAS (16.6%; 95% CI 14.6–18.7; 2 studies; n = 732) and highest using the STAI (49.6%; 95% CI 46.0–53.2; 2 studies; n = 732). One study of postnatal anxiety symptoms (listed as 'Other' in Table 2) used the GHQ and reported a prevalence of 6.5% (95% CI 3.3–12.2). Geographically, the prevalence of antenatal anxiety symptoms was highest in Eastern Europe (42.6%; 95% CI 20.1–55.6; 95% PI 5.2–86.3; I² 97.1%; 6 studies; n = 2254) and Iran (44.9%; 95% CI 29.0–61.4; 95% PI 1.4–94.7; I² 95.5%; 4 studies; n = 865) and lowest in China (17.6%; 95% CI 9.8–27.2; 95% PI 0.0–58.4; I² 99.4%; 9 studies; n = 13,725) and Africa (15.9%; 95% CI 12.7–19.4; 95% PI 6.3–28.7; I² 71.5%; 4 studies; n = 2008). The prevalence of postnatal anxiety symptoms was highest in Eastern Europe (63.4%; 95% CI 57.0–69.4) and lowest in China (15.2%; 95% CI 13.3–17.3). Results of fixed-effects meta-analysis did not differ significantly from random-effects models (SI8). The results of meta-regression analyses including pooled estimates for subgroups based on

perinatal status, instrument, outcome, geographical location and risk of selection, detection and attrition bias are included in SI9. Random-effects meta-regression suggests a lower prevalence of anxiety in studies which used diagnostic interviews compared with those relying on screening tools (8% vs. 26%; p < 0.01). Meta-regression also confirmed differences in prevalence according to geographical region. There was little evidence of an effect on perinatal status (p = 0.31), risk of selection bias (p = 0.25) or risk of attrition bias (p = 0.79) on prevalence of anxiety. There was no evidence of asymmetry in the distribution of standardised prevalence estimates across studies, indicating no evidence of publication bias (SI10).

4. Discussion

4.1. Main findings

This is the first systematic review and meta-analysis to assess the prevalence of perinatal anxiety exclusively in LMICs. We identified 54 studies from LMIC published since 2016, representing a significant increase in research in this field during the past five years. Prior to 2016, a systematic review had identified only 18 studies from LMIC. Our results suggest perinatal anxiety disorders are a significant burden in LMIC (Dennis et al., 2017). Overall, the prevalence of self-reported anxiety symptoms was 29.2% antenatally and 24.4% postnatally, suggesting that approximately one in every four women in LMIC experiences symptoms of anxiety during the perinatal period. When assessed by stage of pregnancy, the prevalence of self-reported anxiety symptoms was 24.7% in the first trimester, increasing to 34.2% in the second trimester and decreasing again to 28.5% in the third trimester. When diagnostic interviews were used, the prevalence of clinically-diagnosed anxiety disorder was 8.1% antenatally and 16.0% postnatally, though the latter estimate is from a single study and is not a pooled estimate.

Our results suggest that the prevalence of self-reported anxiety symptoms is higher in LMIC compared with HIC. Our pooled estimates of 29.2% antenatally and 24.4% postnatally are higher than Dennis et al.'s (2017) HIC estimates of 19.4% and 13.7%, respectively. Among studies which assessed clinically-diagnosed anxiety disorder, the comparison with HIC estimates is less clear. Our estimate of antenatal anxiety disorder of 8.1% is lower than Dennis et al.'s HIC estimate of 13.4%, while our postnatal estimate of 16.0% is higher than Dennis et al.'s (2017) of 8.4%. The very small number of studies upon which these estimates of clinically-diagnosed anxiety are based (five antenatal and one postnatal

Table 2

Prevalence of antenatal and postnatal anxiety by outcome, instrument, region and risk of bias.

	Anxiety symptoms					Anxiety disorder				
	Studies	Sample	Pooled prevalence % (95% CI)	95% PI	I²%	Studies	Sample	Pooled prevalence % (95% CI)	95% PI	I²%
Antenatal										
Outcome										
Any anxiety	–	–	–	–	–	1	100	12.0 (7.0–19.8)	–	–
GAD	–	–	–	–	–	4	1559	7.5 (3.6–12.7)	0.0–31.9	90.0
Instrument										
Diagnostic	–	–	–	–	–	5	1659	8.1 (4.4–12.8)	0.0–27.9	88.1
DASS	3	1641	28.5 (15.3–43.9)	–	–	–	–	–	–	–
GAD-7	4	6878	20.5 (9.5–34.5)	0.0–78.8	99.2	–	–	–	–	–
HADS-A	8	2693	27.2 (20.6–26.3)	6.7–54.8	92.9	–	–	–	–	–
HSCL-25	3	550	22.7 (19.3–26.3)	–	–	–	–	–	–	–
SAS	9	11,352	22.5 (13.7–32.6)	0.0–64.4	99.1	–	–	–	–	–
STAI	4	1804	40.4 (17.1–66.3)	0.0–100.0	99.1	–	–	–	–	–
Other[a]	6	3837	38.7 (29.8–48.0)	7.9–75.7	96.3	–	–	–	–	–
Region										
Africa	4	2008	15.9 (12.7–19.4)	6.3–28.7	71.5	1	376	2.1 (1.1–4.1)	–	–
Latin America	5	6211	28.6 (24.8–32.6)	18.0–40.4	75.9	2	1123	9.6 (7.1–12.4)	–	–
Asia	9	3692	32.0 (26.0–38.2)	10.4–58.7	93.1	2	160	11.8 (7.2–17.4)	–	–
Eastern Europe	6	2254	42.6 (30.1–55.6)	5.2–86.3	97.1	–	–	–	–	–
China	9	13,725	17.6 (9.8–27.2)	0.0–58.4	99.4	–	–	–	–	–
Iran	4	865	44.9 (29.0–61.4)	1.4–94.7	95.5	–	–	–	–	–
Selection bias										
Low risk	8	7978	31.1 (23.7–38.9)	7.0–62.4	97.2	1	975	10.9 (9.0–12.9)	–	–
Moderate risk	4	782	30.0 (19.8–41.3)	2.3–70.5	90.1	1	148	6.1 (3.2–11.2)	–	–
High risk	26	19,995	28.2 (22.0–34.9)	1.7–69.2	99.0	3	536	7.4 (1.1–18.1)	–	–
Attrition bias										
Low risk	33	23,381	30.6 (25.0–36.4)	2.6–71.0	98.8	5	1659	8.1 (4.4–12.8)	0.0–27.9	88.1
Moderate risk	2	988	15.3 (10.5–20.9)	–	–	–	–	–	–	–
High risk	3	4386	26.3 (13.3–41.9)	–	–	–	–	–	–	–
Postnatal										
Outcome										
Any anxiety	–	–	–	–	–	1	706	16.0 (13.5–18.9)	–	–
GAD	–	–	–	–	–	–	–	–	–	–
Instrument										
Diagnostic	–	–	–	–	–	1	706	16.0 (13.5–18.9)	–	–
DASS	2	727	32.0 (28.7–35.4)	–	–	–	–	–	–	–
GAD-7	–	–	–	–	–	–	–	–	–	–
HADS-A	2	576	32.0 (26.9–37.3)	–	37.8	–	–	–	–	–
HSCL-25	1	567	18.7 (15.7–22.1)	–	–	–	–	–	–	–
SAS	2	1281	16.6 (14.6–18.7)	–	–	–	–	–	–	–
STAI	2	732	49.6 (46.0–53.2)	–	–	–	–	–	–	–
Other[a]	1	124	6.5 (3.3–12.2)	–	–	–	–	–	–	–
Region										
Africa	4	1153	32.1 (23.8–41.0)	7.5–63.8	88.1	–	–	–	–	–
Latin America	–	–	–	–	–	1	706	16.0 (13.5–18.9)	–	–
Asia	1	567	18.7 (15.7–22.1)	–	–	–	–	–	–	–
Eastern Europe	1	227	63.4 (57.0–69.4)	–	–	–	–	–	–	–
China	1	1204	15.2 (13.3–17.3)	–	–	–	–	–	–	–
Iran	3	856	30.2 (5.7–63.4)	–	–	–	–	–	–	–
Selection bias										
Low risk	3	700	26.1 (14.9–39.2)	–	92.1	1	706	16.0 (13.5–18.9)	–	–
Moderate risk	1	567	18.7 (15.7–22.1)	–	–	–	–	–	–	–
High risk	6	2740	38.5 (20.5–58.2)	0.0–97.5	99.0	–	–	–	–	–
Attrition bias										
Low risk	10	4007	31.5 (21.2–42.7)	1.4–76.7	98.0	–	–	–	–	–
Moderate risk	–	–	–	–	–	1	706	16.0 (13.5–18.9)	–	–
High risk	–	–	–	–	–	–	–	–	–	–

Abbreviations: *CI* confidence interval; *PI* prediction interval.

Notes: 95% PI and I² statistic inestimable with ≤3 studies. *Italics* indicate only one study in subgroup; these are not pooled.

[a] 'Others' includes General Health Questionnaire (GHQ), Edinburgh Postnatal Depression Scale (EPDS) anxiety subscale, Hamilton Anxiety Rating Scale (HAM-A), Beck Anxiety Inventory (BAI) and Perinatal Anxiety Screening Scale (PASS).

in our review; six antenatal and eight postnatal in Dennis et al.'s review) means these comparisons must be interpreted cautiously.

Comparing our results with previous LMIC estimates, we found that for self-reported anxiety symptoms our antenatal prevalence was lower than Dennis et al.'s LMIC estimate (29.2% vs. 34.4%) but our postnatal prevalence was similar (24.4% vs. 25.9%) (Dennis et al., 2017). Our review's focus on LMIC and the increased number of LMIC studies published during the past five years allowed us to identify and include

significantly more studies in our meta-analysis of LMIC studies. Our estimates of self-reported anxiety symptoms are based on 36 antenatal and 15 postnatal studies, whereas Dennis et al. (2017) are based on only 13 antenatal and five postnatal studies. Our review also includes more geographically diverse samples: we expand upon previous reviews through the addition of studies from which data was previously unavailable, including Colombia, Egypt, Iran, India, Mexico, Nepal, Pakistan, Serbia and Rwanda. We believe that the larger number of

studies included in our review and the greater range of countries represented makes our estimates more robust, comprehensive and up-to-date than previously published estimates. For clinically-diagnosed anxiety disorder our antenatal prevalence of 8.1% (5 studies) was markedly lower than Dennis et al.'s of 18.2% (3 studies), but given the small number of studies across both reviews, these estimates must be considered with caution.

4.2. Results of subgroup analyses

Subgroup analyses highlighted differences in prevalence according to a number of factors including timing during the perinatal period, type of instrument used and geographical setting. While interpreting these results it is important to acknowledge the wide prediction intervals, which suggest that the true prevalence of anxiety may differ greatly according to these factors. Studies which used a diagnostic tool reported significantly lower prevalence of anxiety than those using self-report screening tools. This is unsurprising given that diagnostic tools assess for clinical disorders while screening tools assess for symptoms. Screening tools often have low specificity to detect as many affected individuals as possible, and not all those who screen positive have an anxiety disorder. Screening tools are therefore likely to over-estimate prevalence. Clinical interviews are the gold standard for diagnosing mental disorders and provide more accurate estimates of anxiety disorder prevalence. Levis et al. (2019) conducted a large meta-analysis of depression prevalence and found that pooled prevalence based on screening tools was 31%, compared with a pooled prevalence of 17% based on diagnostic interviews (Levis et al., 2019). This highlights the important of being clear with regards to whether results refer to anxiety disorder or anxiety symptoms.

The variation in prevalence of anxiety symptoms among studies using screening tools (between 20.5%–40.4% antenatally and 6.5%–49.6% postnatally) may be due to differences in specificity and sensitivity as well as different cut-offs applied. There have been few validation studies of anxiety screening tools in LMIC, and subsequently, studies included in our review may have used tools and cut-offs that had not been locally validated (Mughal et al., 2020). Validation within the specific setting is important as mental disorders may present differently depending on cultural context. The use of differing cut-offs across different settings is appropriate provided these cut-offs have been locally validated. Nonetheless, differences in specificity and sensitivity of tools across settings will contribute to heterogeneity that does not necessarily reflect true differences in underlying prevalence. Sometimes, different cut-offs are used to assess anxiety of varying severity. Most studies include moderate and severe anxiety in their overall prevalence of anxiety symptoms. However, others applied lower thresholds and included milder forms of anxiety in their reported prevalence. This is evident, for example, in the five studies using the DASS which used different cut-offs for mild ($\geq$8), moderate ($\geq$10) and severe ($\geq$15) anxiety. Using the cut-off for severe cases risks missing women with clinically-significant moderate anxiety, while using the cut-off for mild cases can make it difficult to identify women most in need of support and overwhelm mental health systems. The SAS and STAI, used by several included studies, are designed for research rather than clinical use. These may be more time-consuming and difficult to use in practice as self-report tools. The STAI identified a proportion of women scoring above the cut-off which was markedly higher than that of other tools. This may further limit its use in clinical practice.

When we explored anxiety prevalence by geographical region, the most striking finding was the lack of studies from low-income countries. Umuziga et al. (2020) assessed perinatal anxiety symptoms in Rwanda, reporting a prevalence of 28.2% antenatally and 48.1% postnatally. This was the only study we identified from a low-income country; all other studies were from middle-income countries. Although Africa, Asia, Latin America and Europe were all represented, over two thirds of studies were conducted in six countries, highlighting the many remaining

geographical gaps. The generalisability of our findings is limited by these gaps. The large number of studies from China and Iran allowed us to calculate pooled prevalence for these countries while others were grouped by region. Anxiety symptoms prevalence was highest in Eastern Europe (42.6% antenatal; 63.4% postnatal) and Iran (44.9% antenatal; 30.2% postnatal) and lowest in Africa (15.9% antenatal) China (17.6% antenatal; 15.2% postnatal) and the rest of Asia (18.7% postnatal). These differences may relate to cultural differences in the experience and manifestation of anxiety. Specifically, cultural practices relating to the perinatal period differ across regions and may be either protective or detrimental to the development of anxiety disorders, depending on the context. Socioeconomic factors may also play a role in these differences by region: levels of poverty and deprivation vary between LMIC, and even within countries, anxiety levels vary by region and socioeconomic profiles of participants.

Limiting our analysis to studies at low risk of selection and attrition bias resulted in no significant changes in prevalence estimates, shifting the antenatal estimate of anxiety symptoms from 29.2% to 30.7% and the postnatal estimate from 24.4% to 24.8%. We did not present results of analyses according to detection bias because these were identical to the analyses of screening instruments vs. diagnostic interviews, which formed the basis of the detection bias measure. Despite subgroup analyses, high statistical heterogeneity remained. Possible explanations for these persisting differences are the inclusion criteria and definitions. For example, most studies excluded 'high risk' women definitions of risk varied: some studies excluded women with pre-existing mental disorders, while others excluded women with any medical conditions or complications of pregnancy. Such exclusions may have led to prevalence being under-estimated. The settings in which individual studies were carried out included hospital as well as community-based healthcare providers and both rural and urban areas. This diversity may also have affected differences in reported prevalence.

4.3. Implications for research and clinical practice

Our study has highlighted the significant burden of anxiety among perinatal women living in LMIC. Our results have implications for clinical practice and suggest that screening of perinatal women for anxiety disorders may be appropriate. In many LMIC settings, competing clinical priorities, time and resource constraints and already overstretched mental health services mean that it is not feasible to administer a clinical interview to every pregnant woman. Screening tools may provide an alternative means to identifying women at risk of anxiety: they are quicker and less resource-intensive to administer, and upon completion a trained healthcare professional can assess women scoring above the cut-off to confirm the diagnosis. Care must be taken when selecting tools which should be validated locally prior to use to ensure acceptability, relevance and validity. It is also important to ensure that appropriate intervention pathways are available locally to support women who are identified as having perinatal anxiety. A number of interventions have been shown to be effective in addressing perinatal mental disorders in LMIC settings (Rahman et al., 2013). Examples of such interventions include cognitive behaviour therapy delivered by trained counsellors in the community, psychoeducational approaches in which information about perinatal mental disorders and support services is provided during antenatal and postnatal classes, and broader parenting education programmes which have indirectly impacted positively upon maternal mood (Rahman et al., 2008; Lara et al., 2010; Morris et al., 2012).

Our findings also demonstrate how variability in methods – particularly the choice of screening tool – can affect prevalence estimates. Efforts should be made to standardise assessment methods and care should be taken when drawing comparisons between results from different tools. Previous research has highlighted the predominance among meta-analyses of perinatal depression of estimates based on screening tools rather than diagnostic interviews (Levis et al., 2019).

Our review confirms that this is also the case for perinatal anxiety. We have identified significant research gaps in low-income countries with very little data on perinatal anxiety available from these settings. Given the variation in anxiety prevalence between countries included in our studies, areas that have not been studied may show significantly different anxiety prevalence. Establishing reliable estimates for individual areas is essential for assessing the burden of anxiety among women living in low-income settings, guide further research and provide evidence for the allocation of mental health resources.

4.4. Strengths and limitations

This is the first systematic review and meta-analysis to focus exclusively on perinatal anxiety in LMIC. Further strengths include our inclusive and comprehensive search strategy with no language restrictions. Limiting ourselves to studies published since January 2016 enabled us to focus on the most recent evidence and compare our results to those of a previous comprehensive review on this topic. Our random-effects meta-analysis enabled us to calculate a pooled prevalence despite heterogeneity between studies and to explore potential causes of heterogeneity through subgroup analyses and meta-regression.

5. Conclusion

This systematic review provides the first comprehensive overview of perinatal anxiety among perinatal women in LMIC. Our results suggest that these disorders represent a significant burden in LMIC, with prevalence estimates higher than those from HIC settings. Although substantial progress has been made in recent years there remain important gaps in our knowledge: in particular, there is a lack of research from low-income (rather than middle-income) countries. Our findings justify further research in these areas and for the advancement in the identification, treatment and support for women living with perinatal anxiety.

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Data availability

Data collection forms, data extraction tables, data used for meta-analyses, analytic code and quality assessment templates are available from the corresponding author on request.

CRediT authorship contribution statement

MNS, GF and FA formulated the research question, developed the search strategy and conducted screening and data extraction. MNS, GF, CO and FA carried out statistical analyses and wrote the article.

Conflict of Interest

All authors declare no conflicts of interest.

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