ORIGINAL ARTICLE



Prevalence of bacterial vaginosis among pregnant women attending antenatal care in low- and middle-income countries between 2000 and 2020: A systematic review and meta-analysis

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Abstract

Background: Bacterial vaginosis increases risk of preterm birth and low birthweight, adverse pregnancy outcomes that disproportionately affect low- and middle-income countries (LMICs).

Objectives: We aimed to estimate the prevalence of bacterial vaginosis among pregnant women attending antenatal care in LMICs between 2000 and 2020.

Search Strategy: We conducted a systematic review of PubMed, Embase and five regional databases.

Selection Criteria: We included studies conducted in LMICs and published between 2000 and 2020 in which bacterial vaginosis prevalence was reported among pregnant women attending antenatal care.

Data Collection and Analysis: We corrected point estimates and applied randomeffects models to generate pool prevalence estimates. We carried out subgroup analyses by study year, country-income level, HIV prevalence, sample size, diagnostic method, trimester of pregnancy, presence of symptoms at diagnosis and risk of bias.

Main Results: Of 1132 publications, 74 studies met inclusion criteria, contributing 80 data points from 46 661 pregnant women. Overall pooled mean prevalence across LMICs was 15.7%. Regional prevalence ranged from 25.1% in sub-Saharan Africa to 7.4% in Central and Southern Asia. Prevalence was 33.4% in studies where HIV prevalence was $\geq 10\%$, and 6.6% in which HIV prevalence was <10%. The prevalence of bacterial vaginosis among pregnant women who were symptomatic was 24.2% versus 11.8% among those without associated symptoms. **Conclusions:** Bacterial vaginosis prevalence is high. World Health Organization guidelines recommend screening and treatment for symptomatic pregnant women who have HIV infection. Research is needed to characterise biological mechanisms of bacterial vaginosis that lead to preterm birth and low birthweight, and to investigate antenatal interventions that may better interrupt these pathways.

K E Y W O R D S

antenatal care, bacterial vaginosis, low- and middle-income countries, pregnant women, prevalence

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INTRODUCTION

Bacterial vaginosis, the most common urogenital disorder in the world, is considered a vaginal dysbiosis that results from an overgrowth of anaerobic bacteria.^{1,2} Although its aetiology is poorly understood,³⁻⁶ bacterial vaginosis is known to increase the risk of acquiring HIV (relative risk of 1.6; 95% confidence interval [CI]: 1.2–2.1),⁷ Herpes Simplex Virus Type 2 (relative risk of 1.55; 95% CI: 1.30-1.84),⁸ Trichomonas vaginalis (adjusted odds ratio of 1.87; 95% CI: 1.45-2.40)⁹ and human papillomavirus (relative risk of 1.33; 95% CI: 1.18-1.50).¹⁰ Gardnerella vaginalis and Prevotella bivia, key markers of bacterial vaginosis, stimulate HIV expression in vitro.^{11,12} Pregnant HIV-infected women with bacterial vaginosis are at greater risk of vertical transmission of the AIDS virus compared to HIV-infected counterparts without bacterial vaginosis.¹³ Adverse pregnancy outcomes associated with bacterial vaginosis include increased risk of spontaneous abortion,^{14,15} preterm delivery^{14,16–19} and low birthweight (<2.5 kg).^{16–18} Preterm delivery remains the leading cause of perinatal morbidity and mortality globally,²⁰ whereas low birthweight newborns experience more cases of respiratory infection and diarrhoeal disease than counterparts born above the 2.5 kg threshold^{21,22} and, in adulthood, are more likely to suffer from micro-vascular conditions.²³⁻²⁵ Low birthweight girls, in their reproductive years, are more likely to develop pre-eclampsia when pregnant and deliver low birthweight babies themselves.²⁶ Thus, reducing the fraction of adverse pregnancy outcomes attributable to bacterial vaginosis may have global implications and contribute substantially to achieving Target 3.2 of the Sustainable Development Goals (SDGs).

We undertook a systematic review and meta-analysis to estimate the prevalence of bacterial vaginosis among pregnant women attending antenatal care in low- and middle-income countries (LMICs) from 2000 to 2020. We conducted sub-group analyses to assess potential variations in the burden of bacterial vaginosis and to inform a review of antenatal care guidelines with the aim of reducing bacterial vaginosis and its consequences in pregnancy.

METHODS

We searched PubMed, Embase and five regional databases under Global Index Medicus: (1) African Index Medicus, (2) Index Medicus for the Eastern Mediterranean Region, (3) Index Medicus for the South-East Asia Region, (4) Health information from Latin America and the Caribbean countries and (5) the Western Pacific Region. We identified additional studies from reference lists. We used the World Bank country classification to define LMICs and to categorise countries based on income in low, lowermiddle and upper-middle-income.²⁷ We applied Cochrane's LMIC filter to search individual LMICs.²⁸ The detailed search-term strategy is included in Supporting Infomation S1: Appendix S1.

Eligibility criteria

Without language restriction, we included studies conducted in LMICs and published between 1 January 2000 and 31 December 2020 in which bacterial vaginosis prevalence was reported among pregnant women attending antenatal care. We excluded studies from high-income countries, and studies that focused exclusively on pregnant women at higher risk of having bacterial vaginosis than a cross-section of antenatal attendees. We included point estimates from multi-year studies that began before 2000 if more than onehalf of the study period was from 2000 onward. If studies included both high-risk and non-high-risk groups and stratified them, we extracted only data from the non-highrisk group. We included published abstracts of conference presentations if they contained information on the number of pregnant women with bacterial vaginosis, sample size, and bacterial vaginosis diagnostic method used. If studies provided the percentage of bacterial-vaginosis-positive women and denominator without a numerator, we calculated the range of possible numerators and chose the midpoint. This systematic review and meta-analysis was registered with PROSPERO (CRD42022248505).

Data selection, management, and extraction

We used Rayyan online²⁹ to facilitate reviewing studies identified through database searches by first importing all records into the platform, removing duplicates, and screening them by title and abstract. We removed studies that failed to meet inclusion criteria, and recorded the reason for their exclusion (Supporting Infomation S1: Figure S1). If a determination could not be made at the level of title and abstract, we retained studies for full-text review. We then exported records into Endnote X9 and completed the eligibility review, recording reasons for study exclusion.

From all eligible studies, we extracted the name of the first author, study country, design, setting, duration and specific year(s). If the year(s) were not available, we used the year of publication instead, noting this in our summary table (Supporting Infomation S1: Table S1). We also extracted data for the study population, sample size, care setting, age range, trimester when tested, number of pregnant women tested and number who tested positive and diagnostic methods used. We also recorded the prevalence of HIV when reported among women tested for bacterial vaginosis and the percentage of symptomatic women among those who were bacterial-vaginosis positive. We used the Appraisal tool for Cross-Sectional Studies (AXIS) to examine the potential risk of bias in studies (Supporting Infomation S1: Table S2).³⁰

Data synthesis

Two co-authors (FJP and ASR) independently completed data extraction. When authors could not agree on whether to include a study or the data to extract, a third coauthor (RMC) served as arbiter. Statistical analyses, including meta-analyses, were conducted using Stata/IC 16. We first calculated uncorrected point estimates (Supporting Infomation S1: Table S1) and then applied a standard method to correct data points based on sensitivity and specificity measures of assays used in each study³¹ (Supporting Infomation S1: Table S3), as done elsewhere.^{4,32,33} If an assay had a reported range of sensitivity or specificity measures, we used the midpoint values for each. If a publication used multiple diagnostic tests, as occurred in studies that evaluated assays, we applied the gold standard sensitivity and specificity that had been used. We then applied random-effects models in Stata using the 'metaprop' command to generate pool prevalence estimates and corresponding 95% confidence intervals (CIs).³⁴ We then generated forest plots of pooled mean prevalence estimates by SDG region. We conducted subgroup analyses for time periods (2000-2009 and 2010-2020), country income level classified by the World Bank (low, lower-middle and uppermiddle-income),²⁷ HIV prevalence (<10% and $\geq 10\%$), sample size (<500 and ≥500), diagnostic method (Nugent scoring, Amsel criteria and BVBlue test), trimester when tested (first, second, third and unreported trimesters), bacterial vaginosis symptoms (asymptomatic and symptomatic) and AXIS score classification (low-, intermediateand high-risk of bias).

RESULTS

Study selection

We identified 1132 records through database searches. After removing duplicates, we screened 951 titles and abstracts, excluding 783 records. We carried out a full-text review of the remaining 168 articles, and determined that 62 studies were eligible for inclusion (Supporting Infomation S1: Figure S1). We identified 12 additional articles from other sources for a total of 74 studies, containing 80 data points for analysis.

Pooled mean prevalence estimates

The overall pooled mean prevalence estimate for bacterial vaginosis was 15.7% (95% CI: 12.2%–19.7%; N = 46 661) (Table 1). From highest to lowest by SDG region, the pooled mean prevalence in sub-Saharan Africa was 25.1% (95% CI: 17.5%–33.6%; N = 23 028 women tested), followed by Latin America and the Caribbean with 22.6% (95% CI: 12.0%–35.4%; N = 4303), Northern Africa and Western Asia at 14.5% (95% CI: 0.0%–58.5%; N = 756), Oceania at

13.6% (95% CI: 8.7%–20.7%; N = 125), Eastern and South-Eastern Asia with 9.4% (95% CI: 3.0%–18.7%; N = 3909), and Central and Southern Asia at 7.4% (95% CI: 4.3%–11.3%; N = 14 540). Prevalence estimates at country level are shown in Figure 1, Supporting Infomation S1: Table S1 and S4. Supporting Infomation S1: Figures S2–S8 display the overall and regional forest plots for the pooled mean prevalence estimates of bacterial vaginosis. The pooled mean prevalence of data points from 2000 to 2009 was 13.3% (95% CI: 9.0%–18.4%; N = 26 331) and 18.1% (95% CI: 12.6%–24.2%; N = 20 330) from 2010 to 2020 (Figure 2 and Table 1).

We identified data points for all SDG regions in both decades with the exception of Northern Africa and Western Asia, and Oceania which had estimates only for the more recent decade. Sub-Saharan Africa had the highest number of pooled mean prevalence estimates for all time periods: 19.5% (95% CI: 10.6%-30.2%; N = 16 130) from 2000 to 2009, 29.2% (95% CI: 22.6%–36.2%; N = 6898) from 2010 to 2020, and 25.1% (95% CI: 17.5%–33.6%; *N* = 23 028) overall. Subgroup analyses are presented in Table 2. When stratified by income, the highest prevalence was in upper-middleincome countries with 21.7% (95% CI: 15.1%-29.2%; N = 10 211), followed by low-income countries at 20.5% (95% CI: 4.9%-42.9%; N = 3765), and then 12.4% (95% CI: 8.6%-16.8%; N = 32685) in lower-middle-income countries. Just over one third of studies (35.1%) also reported HIV prevalence data alongside bacterial vaginosis prevalence estimates. In antenatal settings where the HIV prevalence was $\geq 10\%$, the pooled mean prevalence of bacterial vaginosis was 33.4% (95% CI: 12.3%–58.8%; N=4782) versus 6.6% (95% CI: 1.8%-14.2%; N = 11 600) where HIV prevalence was <10%. The pooled mean prevalence of bacterial vaginosis was 18.8% (95% CI: 14.4%-23.6%; N = 12 356), where the sample size was <500 and 10.3% (95% CI: 5.7%–16.0%; N = 34 305) among studies with a sample size of \geq 500. When stratifying bacterial vaginosis prevalence estimates by diagnostic method, the range was from 19.0% (95% CI: 14.6%–23.7%; N = 30 402) for Nugent scoring to 6.4% (95% CI: 2.6%–11.6%; *N* = 16 134) with Amsel criteria. Point-of-care BVBlue tests were used among pregnant women for just one prevalence data point, 13.6% (95% CI: 8.7%–20.7%; N = 125). The pooled mean prevalence of bacterial vaginosis in the first and second trimesters was 14.3% (95% CI: 6.4%–24.5%; N = 7100) and 14.1% (95% CI: 8.2%–21.4%; N = 13 104), respectively. When women were tested just in the third trimester, the pooled mean prevalence was 8.9% (95% CI: 0.8%-23.8%; N = 2698). Among studies that had not stratified the trimester of bacterial vaginosis testing, the pooled mean prevalence was 20.3% (95% CI: 10.3%–32.6%; N = 7666). The pooled mean prevalence of bacterial vaginosis among pregnant women who were symptomatic was 24.2% (95% CI: 17.0%-32.2%; N = 13 325), in contrast to 11.8% (95% CI: 5.5%-19.9%; N = 5441) among those who were without symptoms associated with bacterial vaginosis. 55.6% (15 out of 27 data points), where less than 50% of women reported

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TABLE 1 Pooled estimi 2000 and 2020.	ates of bacteria	l vaginosis among pre	egnant women attending ante:	natal care facilities in low- ar	ıd middle-inco	me countries by r	egions of the Sus	tainable Developm	nent Goals between
Regions	Number positive	Number tested (% of total)	Uncorrected pooled estimates (95% CI)	Corrected pooled estimates (95% CI)	Median cases	Sample size range	Countries	Data points (% of total)	Heterogeneity* <i>T</i> ²
2000-2020									
Sub-Saharan Africa	5051	23 028 (49.3%)	29.2% (24.9%–33.5%)	25.1% (17.5%–33.6%)	113.5	30-3950	14	32 (40.0%)	99.2%
Latin America and the Caribbean	973	4303 (9.2%)	25.8% (10.7% - 40.8%)	22.6% (12.0%–35.4%)	60	120-1699	4	8 (10.0%)	98.7%
Northern Africa and Western Asia	205	756 (1.6%)	24.0% (0.0%-51.8%)	14.5% (0.0% - 58.5%)	26	15-520	ε	3 (3.8%)	99.1%
Oceania	22	125 (0.3%)	17.6%	13.6% (8.7%-20.7%)	22	125-125	1	1 (1.2%)	NA
Eastern and South- Eastern Asia	666	3909 (8.4%)	15.8% (9.8%–21.9%)	9.4% (3.0%–18.7%)	31.5	60-761	~	12 (15.0%)	98.6%
Central and Southern Asia	1805	14 540 (31.2%)	14.9% (10.9%–18.9%)	7.4% (4.3%–11.3%)	60	102-4201	IJ	24 (30.0%)	98.4%
Total	8722	46 661	22.2% (19.3%-25.1%)	15.7% (12.2%-19.7%)	51	15-4201	34	80	99.2%
2010-2020									
Sub-Saharan Africa	2153	6898 (33.9%)	30.1% (25.0%–35.3%)	29.2% (22.6%–36.2%)	67	30-1304	10	19 (45.2%)	97.3%
Latin America and the Caribbean	370	1755 (8.6%)	33.7% (0.0%–69.4%)	32.5% (7.9%–64.0%)	06	120-1214	°	4 (9.5%)	99.2%
Northern Africa and Western Asia	205	756 (3.7%)	24.0% (0.0%-51.8%)	14.5% (0.0% - 58.5%)	26	15-520	ς	3 (7.2%)	99.1%
Oceania	22	125 (0.6%)	17.6%	13.6% (8.7% - 20.7%)	22	125-125	1	1 (2.4%)	NA
Eastern and South- Eastern Asia	426	2085 (10.3%)	17.5% (0.0%-41.4%)	7.9% (0.0%–33.7%)	62	60-761	7	4 (9.5%)	99.5%
Central and Southern Asia	838	8711 (42.9%)	11.6% (6.6%–16.5%)	5.0% (2.0%–9.2%)	34	131-4201	4	11 (26.2%)	97.8%
Sub-total	4014	20 330	23.7% (19.3%-28.0%)	18.1% (12.6%-24.2%)	50.5	15-4201	23	42	99.1%
2000-2009									
Sub-Saharan Africa	2898	16 130 (61.3%)	27.8% (19.3%-36.3%)	$19.5\% \ (10.6\% - 30.2\%)$	139	48-3950	8	13 (34.2%)	99.6%
Latin America and the Caribbean	603	2548 (9.7%)	17.9% (3.0%-32.8%)	14.4% $(4.8% - 27.8%)$	56	155-1699	2	4 (10.5%)	98.0%
Northern Africa and Western Asia	IN	IN	IN	IN	IN	IN	IN	IN	IN

symptoms were from sub-Saharan Africa. Among these symptomatic cases, approximately one third were positive for BV. In terms of AXIS risk of bias classification, the prevalence was 21.4% (95% CI: 12.6%-31.7%; N = 12 594) among studies considered at low risk, followed by 16.6% (95% CI: 10.9%-23.2%; N = 22 061) for intermediate risk, and 12.3% (95% CI: 7.4%-18.1%; N=12 006) in studies considered high risk.

DISCUSSION

Main findings

The prevalence of bacterial vaginosis among pregnant women attending antenatal care facilities between 2000 and 2020 in LMICs was high. The overall prevalence estimate was dominated by data from two SDG regions: sub-Saharan Africa and Central and Southern Asia. For meta-analysis, sub-Saharan Africa contributed 40.0% (32/ 80) of all data points, and nearly one half of pregnant women tested for bacterial vaginosis, 49.3% (23 028/46 661). The sub-Saharan region also had the highest pooled mean prevalence of bacterial vaginosis at 25.1% which could have skewed the combined LMIC pooled mean prevalence estimate higher. However, the Central and Southern Asia region may have off-set this for having contained the second most data points in our meta-analysis, 30% (24/80), representing 31.2% (14 540/46 661) of all pregnant women included, and had the lowest prevalence of bacterial vaginosis among SDG regions at 7.4%. Consequently, our pooled mean prevalence of 15.7% may reflect the true burden of bacterial vaginosis in pregnancy across LMICs, as well as within these two SDG regions specifically. Of note, the pooled prevalence estimate for the Central and Southern Asia region is heavily weighted by one large multi-year study in Bangladesh which represented 30% (4201/14 033) of all women tested in the SDG region. The corrected point prevalence estimate was 5.8%, which lowered the pooled regional estimate.

Variation in prevalence across SDG regions may have a biological basis as the vaginal microbiome differs around the world.³⁵ Although the composition of species associated with bacterial vaginosis across countries of sub-Saharan Africa has been reported to be similar, the presence of protective species including Lactobacillus crispatus and L. vaginalis in women with a normal Nugent scores appeared to be lower compared to studies conducted in other SDG regions.³⁵ Cultural-behavioural factors such as vaginal douching, number of sexual partners, use of intrauterine devices, and poverty may also contribute to differences,^{36–38} alongside genetic factors.⁵ Our subgroup analyses suggest there are true differences in bacterial vaginosis prevalence related to HIV prevalence (p < 0.001), diagnostic method used (p < 0.001) and symptoms (p = 0.01). Our study did not, however, detect meaningful differences per trimester of diagnosis. This may be due to a lack of prevalence data from

TABLE 1 (Continued)

Regions	positive	(% of total)	estimates (95% CI)	contected pooled estimates (95% CI)	cases	sample size	Countries	Data pounts (% of total)	I^2
Oceania	IN	IN	IN	IN	IN	IN	IN	IN	IN
Eastern and South- Eastern Asia	240	1824 (6.9%)	15.0% (9.5%–20.5%)	10.0% (5.3% - 15.9%)	31.5	121-505	IJ	8 (21.1%)	92.9%
Central and Southern Asia	967	5829 (22.1%)	17.8% (11.5%–24.0%)	9.8% (4.2%–17.4%)	60	102-1233	ъ	13 (34.2%)	98.6%
Sub-total	4708	26 331	20.6% (16.7%-24.5%)	13.3% (9.0%-18.4%)	55.5	48-3950	20	38	99.2%
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^tHeterogeneity testing in all instances produced a ρ value of <0.001



FIGURE 1 Map of bacterial vaginosis prevalence estimates in pregnancy by low- and middle-income country between 2000 and 2020.



FIGURE 2 Pooled bacterial vaginosis prevalence estimates among pregnant women attending antenatal care in low- and middle-income countries by regions of the Sustainable Development Goals between 2000 and 2020. Uncertainty bars in black reflect 95% confidence intervals.

early pregnancy; only 10% of our data points were from the first trimester. Prior studies have shown the prevalence of bacterial vaginosis to be highest in the first trimester of pregnancy, declining to term.^{1,39,40} This is consequential given that women with bacterial vaginosis in the first trimester face an increased risk of adverse pregnancy

outcomes, including second-trimester pregnancy loss and preterm delivery.^{41,42} Where HIV prevalence was $\geq 10\%$ in the antenatal population, one third of all pregnant women had bacterial vaginosis. This suggests the potential public health utility of providing universal bacterial vaginosis screening for all pregnant women in antenatal care facilities

TABLE 2 Subgroup anal Development Goals between	yses of bacteri 2000 and 202	al vaginosis prevalence 0.	estimates among pregnant	women attending antenatal o	are facilities ii	n low- and middl	e-income count	ries by regions of	the Sustainable
Subgroups	Number positive	Number tested (% of total)	Uncorrected pooled estimates (95% CI)	Corrected pooled estimates (95% CI)	Median cases	Sample size range	Countries	Data points (% of total)	Heterogeneity* I^2
Country income level									
Upper-middle	2516	10 211 (21.9%)	26.0% (20.0%-32.0%)	21.7% ($15.1% - 29.2%$)	52	30-1699	10	25 (31.3%)	98.7%
Low	600	3765 (8.1%)	25.1% (6.7% $-43.6%$)	20.5% $(4.9% - 42.9%)$	124.5	247-2133	Ŋ	6 (7.5%)	99.4%
Lower-middle	5606	32 685 (70.0%)	19.9% (16.7% - 23.2%)	$12.4\% \ (8.6\% - 16.8\%)$	50	15-4201	19	49 (61.3%)	99.2%
HIV prevalence									
≥10%	1457	4782 (10.2%)	37.3% (22.7%–51.9%)	33.4% (12.3%-58.8%)	209	48-2008	9	7 (8.7%)	99.6%
Not reported	5577	30 279 (64.9%)	21.1% (18.1%-24.1%)	$15.1\% \ (11.5\% - 19.1\%)$	44	15-4201	30	67 (83.8%)	98.8%
<10%	1688	11 600 (24.9%)	16.8% (9.5% - 24.0%)	6.6% (1.8% - 14.2%)	302	125-3950	Ŋ	6 (7.5%)	99.4%
Sample size									
<500	2896	12 356 (26.5%)	23.8% (20.3%-27.4%)	$18.8\% \ (14.4\% - 23.6\%)$	39	15-486	26	54 (67.5%)	97.7%
≥500	5826	34 305 (73.5%)	18.8% (13.8% - 23.9%)	10.3% (5.7% - 16.0%)	178.5	502-4201	18	26 (32.5%)	99.6%
Diagnostic method									
Nugent	5846	30 402 (65.1%)	23.1% (19.6%-26.6%)	$19.0\% \ (14.6\% - 23.7\%)$	49.5	15-4201	29	62 (77.5%)	99.0%
BVBlue test	22	125 (0.3%)	17.6%	13.6% (8.7%-20.7%)	22	125-125	1	1 (1.2%)	NA
Amsel	2854	16 134 (34.6%)	19.3% (13.9%-24.6%)	6.4% $(2.6% - 11.6%)$	76	60-3950	10	17 (21.3%)	99.2%
Trimester									
Mixed trimesters ^a	1539	7666 (16.4%)	25.4% (17.2%-33.7%)	$20.3\% \ (10.3\% - 32.6\%)$	54	60-2133	13	15(18.8%)	99.3%
Trimester not reported	2980	$16\ 093\ (34.5\%)$	24.3% (18.6% - 30.0%)	$17.8\% \ (10.9\% - 25.9\%)$	79.5	15-3950	13	22 (27.5%)	99.3%
1st trimester	1078	7100 (15.2%)	18.8% (11.1% - 26.4%)	$14.3\% \ (6.4\% - 24.5\%)$	34	30-4201	8	8 (10.0%)	98.7%
2nd trimester	2605	13 104 (28.1%)	20.1% (14.8% - 25.3%)	14.1% (8.2% - 21.4%)	50.5	120-1304	17	28 (35.0%)	99.2%
3rd trimester	520	2698 (5.8%)	18.2% (5.8% - 30.5%)	8.9% (0.8%-23.8%)	44	131-691	7	7 (8.7%)	99.1%
Symptoms									
Symptomatic	3156	13 325 (28.5%)	28.4% (23.2%-33.6%)	24.2% (17.0% - 32.2%)	64	30-4201	19	27 (33.8%)	99.0%
Asymptomatic	945	5441 (11.7%)	17.5% (8.5%–26.4%)	11.8% (5.5%–19.9%)	27	48-1699	6	13 (16.2%)	98.4%
Not reported	4621	27 895 (59.8%)	19.2% (15.5%–22.9%)	12.0% (8.0%–16.7%)	61.5	15-3950	17	40 (50.0%)	99.2%
AXIS score classification ^b									

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Subgroups	Number positive	Number tested (% of total)	Uncorrected pooled estimates (95% CI)	Corrected pooled estimates (95% CI)	Median cases	Sample size range	Countries	Data points (% of total)	Heterogeneity* <i>I</i> ²
Low	2487	12 594 (27.0%)	25.5% (18.9% - 32.1%)	21.4% (12.6% - 31.7%)	117	30-4201	12	15 (18.7%)	99.4%
Intermediate	4047	22 061 (47.3%)	23.0% (17.8% - 28.2%)	$16.6\% \ (10.9\% - 23.2\%)$	44	48-3950	21	35 (43.8%)	99.3%
High	2188	12 006 (25.7%)	$19.7\% \ (15.6\% - 23.7\%)$	12.3% (7.4% - 18.1%)	51	15-1541	15	30 (37.5%)	98.7%
Sub-totals	8722	46 661	22.2% (19.3%-25.1%)	15.7% (12.2%-19.7%)	51.5	15-4201	34	80	99.2%
*Heterogeneity testing in all inst	tances produced	a p value of <0.001.							

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^aMixed trimesters refer to studies that did not stratify results.

Overall scores were divided into high risk (<10 criteria), intermediate risk (11-13 criteria) or low (>14 criteria) risk of bias; higher scores indicated higher quality.

where HIV prevalence is high, or at minimum providing bacterial vaginosis testing and treatment to all HIV-infected pregnant women. Additional study is needed to determine which antennal care settings this approach may be costeffective. We found bacterial vaginosis to be three times higher where Nugent scoring was used in contrast to Amsel criteria. This difference in diagnostic methods is higher than expected, although Nugent scoring has been shown to be slightly more predictive of bacterial vaginosis than Amsel.⁴³ Regardless, these differences may simply reflect true variations in underlying prevalence. We found the prevalence of bacterial vaginosis to be twofold higher among symptomatic pregnant women compared to asymptomatic counterparts. This is not surprising given that bacterial vaginosis is the most frequent cause of vaginal discharge among women,^{6,44-48} with approximately 50% of women with bacterial vaginosis experiencing symptoms including vaginal discharge, itching and malodour.44,46

Strengths and limitations

Our study was strengthened by applying a standard method for correcting prevalence data to make them more comparable across studies before pooling in random effects models. Regardless, our pooled mean prevalence estimates probably still underestimate the true burden given that one tenth of data were from women in their first trimester, a time when the prevalence of bacterial vaginosis tends to be most common. Bacterial vaginosis increases the chances of first-trimester spontaneous abortion,^{14,15} cases that would be under-reported in the published prevalence estimates we identified. Another limitation is that there are likely fewer data points closer to the latter part of the recent decade, specifically around 2020, due to inherent delays in publishing those data points. Although we did not have language restrictions, there is a potential for language bias since there may be available data in countries where data are not published because records are not held in a major language. We also acknowledge that publication bias may affect our findings due to the overrepresentation of sub-Saharan Africa, which accounted for 41.2% of the countries and 40.0% of the point prevalence data in our study. While we adjusted for sensitivity and specificity to mitigate this, the overrepresentation could still elevate global prevalence estimates.

Interpretation

To the best of our knowledge, this is the most comprehensive study of bacterial vaginosis prevalence during pregnancy in LMICs to date, spanning two decades with data from 74 studies and 46 661 pregnant women. A metaanalysis by Peebles et al. covered a similar period, 1996 to 2017, and also corrected data points based on the sensitivity and specificity of specific diagnostic assays that had been

used.⁴ However, we searched seven databases in total, compared to just two, which gave us more than double the number of studies, 74 versus 35, with nearly twice as many of pregnant women, 46 661 versus 24 311. This higher yield allowed us to conduct meaningful sub-group analyses, particularly among symptomatic versus asymptomatic cases and HIV-infected versus HIV-uninfected pregnant women. Velu et al. also conducted a systematic review and meta-analysis that included bacterial vaginosis among pregnant women in LMICs. They identified 11 studies that were published between 1997 and 2010 and involving 20 356 pregnant women, but they did not correct data points before combining them in meta-analysis.⁴⁹

The management of bacterial vaginosis is difficult with recurrence posttreatment being very common within 3-12 months.⁵⁰⁻⁵² Recurrent bacterial vaginosis is difficult to treat and requires extended courses of antibiotic therapy for a longlasting cure.^{1,6,51–53} Testing 1 month after treatment is important for ensuring a cure.⁵⁴ Pregnant women should be informed of the potential recurrence of bacterial vaginosis and be tested again. Despite these best practices, current WHO guidelines only recommend bacterial vaginosis screening for symptomatic pregnant women.55 HIV-infected pregnant women should be offered screening and treatment as part of standard antenatal care based on our HIV sub-group analysis and prior evidence that HIV-infected pregnant women with bacterial vaginosis are at greater risk of transmitting the AIDS virus to their newborn compared to HIV-infected counterparts without bacterial vaginosis.

Higher rates of sexually transmitted infections (STIs) in sub-Saharan Africa, especially among pregnant women, may contribute to the increased prevalence of BV. This suggests that symptomatic BV could be more common in this region due to concurrent STIs that cause vaginal discharge. Thus, co-infections with STIs necessitate more holistic care approaches to better understand and manage reproductive health in these populations.

Many research gaps remain, including the evaluation of screen-and-treat approaches for asymptomatic bacterial vaginosis among pregnant women who are at increased risk for preterm delivery. This will necessitate studies that focus on asymptomatic bacterial vaginosis among pregnant women who have a history of preterm delivery and other risk factors, including cervical insufficiency, multifetal gestation, young or advanced maternal age and low maternal body mass index (<20).⁵⁶ Furthermore, studies should evaluate treatment success and have sufficient power to detect a reduction of all-cause preterm delivery.⁵⁶ Due to the biochemical and hormone shifts during pregnancy, more research is also needed to validate the accuracy of bacterial vaginosis screening tests within the pregnant population.⁵⁶ Finally, our current first-line therapies for bacterial vaginosis remain inadequate. Further research is needed to identify interventions that are more effective at reducing G. vaginalis infection without inhibiting Lactobacilli colonies.

CONCLUSION

The pooled mean prevalence of bacterial vaginosis was high among pregnant women attending antenatal care in LMICs. One quarter of pregnant women in sub-Saharan Africa had bacterial vaginosis, and more than one-in-five women did in Latin America and the Caribbean. The greatest burden of bacterial vaginosis was found at healthcare facilities where HIV was also high, suggesting a guideline review is warranted for bacterial vaginosis management among HIV-infected pregnant women.

AUTHOR CONTRIBUTIONS

R. Matthew Chico conceived the idea for the study. Faith Jiyeong Park was responsible for the protocol development and database searches. Faith Jiyeong Park and Aliona S. Rosca independently conducted data extraction. Faith Jiyeong Park and R. Matthew Chico wrote the first draft of the manuscript. Faith Jiyeong Park, Aliona S. Rosca, Piet Cools and R. Matthew Chico interpreted the data and critically reviewed the manuscript. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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CONFLICT OF INTEREST STATEMENT The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

All data used in the study are from publicly available sources.

ETHICS STATEMENT

The study protocol was reviewed by the Research Governance and Integrity Office of the London School of Hygiene & Tropical Medicine (25326/RR/22356). No additional approval was required.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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