GLOBAL HEART

Routine Antenatal Echocardiography in High-Prevalence Areas of Rheumatic Heart Disease: A WHO-Guideline Systematic Review

REVIEW

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ABSTRACT

Background: Rheumatic Heart Disease (RHD) is the most common cause of valvular heart disease worldwide. Undiagnosed or untreated RHD can complicate pregnancy and lead to poor maternal and fetal outcomes and is a significant factor in non-obstetric morbidity. Echocardiography has an emerging role in screening for RHD. We aimed to critically analyse the evidence on the use of echocardiography for screening pregnant women for RHD in high-prevalence areas.

Methods: We searched MEDLINE and Embase to identify the relevant reports. Two independent reviewers assessed the reports against the eligibility criteria in a double-blind process.

Results: The searches (date: 4 April 2023) identified 432 records for screening. Ten non-controlled observational studies were identified, five using portable or handheld echocardiography, comprising data from 23,166 women. Prevalence of RHD varied across the studies, ranging from 0.4 to 6.6% (I^2, heterogeneity >90%). Other cardiac abnormalities (e.g., congenital heart disease and left ventricular systolic dysfunction) were also detected <1% to 2% of cases. Certainty of evidence was very low.

Conclusion: Echocardiography as part of antenatal care in high-prevalence areas may detect RHD or other cardiac abnormalities in asymptomatic pregnant women, potentially reducing the rates of disease progression and adverse labor-associated outcomes. However, this evidence is affected by the low certainty of evidence, and lack of studies comparing echocardiography versus standard antenatal care.

Prospective Registration: PROSPERO 2022 July 4; CRD42022344081 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=344081.

Research question: 'In areas with a high prevalence of rheumatic heart disease, should handheld echocardiography be added to routine antenatal care?'

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in high RHD prevalence areas is still uncertain. This systematic review will critically analyse the available evidence on the use of transthoracic echocardiography (handheld, portable, and non-portable) for screening pregnant women for RHD in high-prevalence areas.

METHODS

This systematic review was performed to address one of the questions (Question 11) of the World Health Organization Update of Guidelines on Prevention and Management of ARF and RHD: 'In areas with a high prevalence of RHD: should handheld echocardiography be added to routine antenatal care?'

ORIGINAL PROTOCOL

The detailed protocol was pre-published on PROSPERO – 2022/CRD42022344081 [19], and available as supplementary material (Annex 1). We did not identify any studies comparing routine antenatal screening with echocardiography versus standard antenatal care. Consequently, we were not able to assess the diagnostic test accuracy of echocardiography vs standard antenatal care for detecting RHD in pregnancy in high prevalence areas or assess the impact of this approach on pregnancy-related outcomes.

MODIFIED PROTOCOL

After discussion with the Guideline Committee in March 2023, it was accepted that the inclusion criteria and study design would have to be broadened so observational studies using handheld echocardiography, or any other form of echocardiography (i.e., standard echocardiography), in the absence of a control group would also be considered eligible. This change aimed to gain further knowledge on the rate of important cardiac findings obtained through echocardiographic screening in pregnancy in high-prevalence populations.

The population of interest for this review was: pregnant women in areas with high prevalence of RHD; we used the data from Watkins et al. 2017 [20] to define high-prevalence areas. The Index Test was echocardiography during routine antenatal care. No comparator or reference test was required. The outcomes of interest were:

- Carditis in ARF, based on revised Jones Criteria by American Heart Association [13], or other criteria locally in use at the time of the study
- RHD, based on the 2012 World Heart Federation (WHF) criteria for echocardiographic diagnosis [14], or other criteria locally in use at the time of the study
- Adverse events (deaths, obstetrics complications, other)
- Time to diagnosis
- Acceptability to provider and patient

Studies were eligible for the purpose of this systematic review when describing findings of echocardiographic screening in pregnant women in areas of high prevalence of RHD. No age restrictions were applied. Studies not reporting on echocardiographic findings were not considered eligible.

Searches were run, documented, and reported by a senior information specialist (FS) on Embase via Ovid SP (1974–present) and MEDLINE via Ovid SP (1946–present). The original search strategy for diagnostic test accuracy studies is described in detail in Appendix 1 and 2 (Supplementary Material). This was subsequently revised and rerun on 4 April 2023, using the search terms 'Pregnan*' and 'Echocardiogr*' and 'Rheumatic', also targeting non-controlled, prevalence studies.

The search results were imported into EndNote 20. After removal of duplicates, the remaining records were then imported into Rayyan, for double-blind screening by two reviewers (SS & SACA). The blinding was inactivated when the screening was finished to resolve the conflicts by a third reviewer (MA).

The following data were extracted from all studies (MA) and double-checked by an independent reviewer (RP).

- Study characteristics: authors, year of publication, country, study design, sample size, study period, setting, patient selection (random/consecutive), follow-up period.
- Patient characteristics: patient type, age, sex, highest level of education, presence of cardiovascular risk factors (hypertension, diabetes mellitus), HIV status, known cardiac disease, gestational age, gestation number, primigravida, presence of symptoms, or New York Heart Association functional status.
- Index test details: Handheld echography device used (type – handheld, portable, stationary device; model), level of experience of the sonographer, screening protocol, and diagnostic criteria.
- Outcomes: Carditis-ARF, RHD, any adverse event (deaths, complication), time to diagnosis, and acceptability to provider and patient
- Other echocardiographic findings, n and%: left ventricular (LV) systolic dysfunction (reported as LV ejection fraction value, class, or other utilized measure), LV hypertrophy, right ventricular dilation, and presence and severity of mitral regurgitation, mitral stenosis, aortic regurgitation, aortic stenosis, and pulmonary hypertension. Data on detection and type of congenital heart disease were also extracted.

We contacted the authors of the studies on an as-required basis to obtain the data or information.

Quality assessment of studies was done by two researchers (SS & MA) using the Newcastle Ottawa scale, which comprises three domains: selection, comparability, and outcome/exposure [21]. Studies were classified as low, moderate, or high quality according to the following criteria: studies scoring a total of 7 to 8 were considered low risk of bias; studies with a score of 6 were considered to have a medium risk of bias; studies scoring 5 points or less were considered to have a high risk of bias. With respect to selection, studies were considered to have a low, medium, or high risk of bias if they scored 3, 1 to 2, or 0 points, respectively [22]. With respect to comparability, studies were considered to have a low, medium, or high risk of bias if they scored 2, 1 or 0 point, respectively. Finally, with respect to outcome, studies scoring 3, 2, or 1 point, were, respectively, considered to have a low, medium, or high risk of bias. Disagreements between the two researchers were resolved by consensus or via a third party (RP).

Statistical heterogeneity was quantified using the I^2 statistic, which describes the percentage of total variation across studies due to heterogeneity rather than chance. Values of <25%, 25% to 50%, and >50% are by convention classified as low, moderate, and high degrees of heterogeneity, respectively.

We summarised % rates with 95% confidence intervals across studies in a forest plot. Meta-analysis using a random-effects model was planned if heterogeneity as per I^2 was not considered high (i.e., if $I^2 < 50\%$) [23]. Funnel plots were used for evaluating the presence of publication bias and traced for outcomes of interest including ≥10 studies [24].

RESULTS

The searches identified 4,565 records, but we were unable to find any controlled studies looking at handheld echocardiography versus standard transthoracic echo or standard clinical care to diagnose RHD in pregnant women (Figure S-1; Supplementary Material). Following the revision of the inclusion criteria in the abovementioned WHO Guideline Committee meeting (March 2023), a new search on 4 of April 2023 yielded additional 432 records for screening. Ten non-controlled observational studies were identified using echocardiography for screening of cardiac disease in pregnant women from high prevalence areas of RHD [25–34], five using portable or handheld echocardiography [25–29] (Figure 1). One study [30] was published as abstract, and the remaining as full text. Four studies were conducted in sub-Saharan Africa [25–26, 28, 31], four studies were conducted in India [29–30, 32, 34], one in Brazil [27] and one in Turkey [33]. The sample sizes were highly variable, ranging from 300 [32] to 14,275 [34], with a combined total of 23,166 women across studies.

In one study all approached women accepted to participate [25]. In Nascimento et al. nearly 50% of women with positive findings on the screening echo failed to attend the recommended follow-up echocardiogram despite the multiple contact attempts [27]. In Snelgrove et al., of

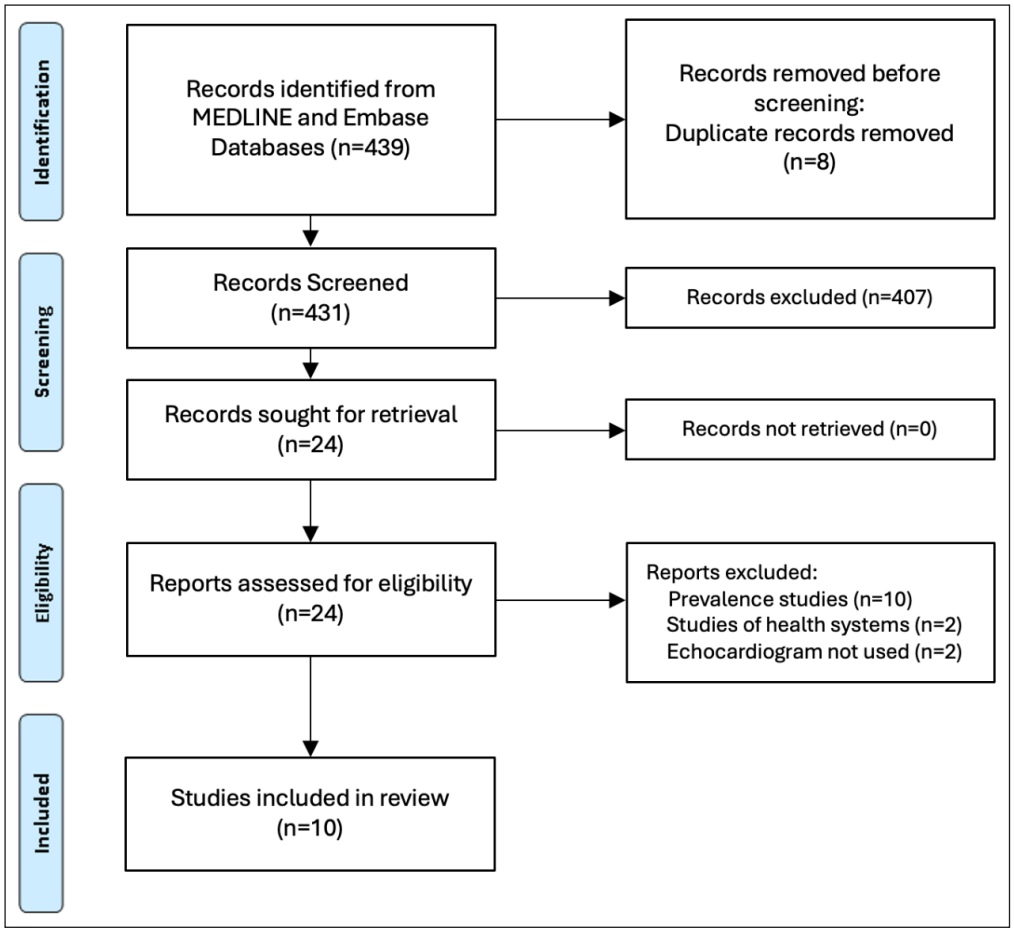

Figure 1 PRISMA flow diagram.

810 potentially eligible women, only 601 consented and accepted to undergo echocardiography [28]. No other studies provided information on acceptability to patent of provider.

Demographic information for the included women is shown in Table 1. Maternal age was consistent throughout the studies, as were pre-existing medical co-morbidities. Maternal HIV status was recorded in two of the studies. Mean gestational age was similar in four of the studies, with most women being scanned in the second or third trimester. Four studies were single-centre studies conducted in a tertiary maternity care setting [28, 30, 33–35]. The remainder were multi-centre studies, coordinated across several clinics in a single city [26] or several states [27, 29]. Two studies had no participants with known cardiac disease at baseline [25, 33], two studies had less than 1% [26–27], and two [29, 30] had up to 5% of pregnant women with known disease at baseline. Bozkaya et al. only recruited women in the first trimester [33]. In three studies most women had an echocardiogram between the 22nd and 25th week of gestation [26–28]. In Otto et al. most echocardiograms were performed at 30 weeks or later [25]. Alshaqri et al. was the only study to also include post-partum women in the analysis [29].

Echocardiography was conducted as part of antenatal care in all studies. The images were acquired by operators and interpreted with a variety of experience. Otto et al. [25] and Beaton et al. [26] used specially trained medical students and nurses, respectively, while Snelgrove et al. [28] used an accredited sonographer. The acquired images were then locally reviewed by cardiologists or trained sonographers [25–26, 28]. Alsharqi et al. [29] employed trained obstetricians and Nascimento et al. [27] used healthcare workers to acquire the images. These two studies exported DICOMs internationally for remote analysis by experts. Echocardiography was performed by a cardiologist in Bozkaya et al. [33].

Scanning protocols differed among the studies, with Nascimento et al. adapting a simplified seven- view echocardiographic protocol for handheld devices, and Alsharqi et al. using the MaatHRI focused image acquisition protocol (Table 2). The criteria used for diagnosis of RHD were not uniform. Four studies [26, 28, 31, 33] used the 2012 WHF criteria for the echocardiographic diagnosis of RHD [14] (Table 3). Otto et al. [25] conducted their study prior to the development of these criteria but used similar morphological abnormalities for diagnosing RHD. Two studies [27, 29] used criteria from the American Society of Echocardiography. The remaining studies did not define the echocardiographic criteria for RHD diagnosis.

Table 1 Demographic and obstetric data.

STUDY ID	COUNTRY	DESIGN	SETTING	SAMPLE SIZE	AGE (YEARS) (MEAN ± SD)	HIGHEST LEVEL OF EDUCATION	HYPERTENSION, n (%)	DIABETES, n (%)	HIV n (%)	KNOWN CARDIAC DISEASE n (%)	GESTATIONAL AGE AT FIRST VISIT, WEEKS (MEAN SD)	PRIMIGRAVIDA, n (%)
Studies using Handheld or Portable Echocardiography												
Otto 2011	Eritrea	Prospective cross sectional	4 clinics in single city	348	26.9 (±6)	NA	0	NA	NA	0	30.9 ± 6.7	NA
Beaton 2019	Uganda	24-month prospective longitudinal investigation	2 health centres, 1 regional referral hospital	3506	24.09 (N/A)	University Degree: 87 (2.5%)	6 (1.7%)	NA	141 (4.0%)	2 (0.06%)	24 (median)	359 (10.2%)
Nascimento 2021	Brazil	13-month prospective longitudinal investigation	22 primary care centres	1112	27 ± 8 years	NA	50 (4.5%)	27 (2.4%)	NA	9 (0.8%)	22 ± 9	NA
Snelgrove 2021	Kenya	Cross sectional study	Antenatal clinic at tertiary maternity centre	601	26.6 years (SD 5.7)	University degree: 82 (13.6%)	1 (0.2%)	1 (0.2%)	45 (7.5%)	27 (4.5%)	25.3 ± 9.5	NA
AlSharqi 2022	India	cross sectional study	10 hospitals across three states-India	301	25.4 (18–42)	University degree: 31 (10.6%)	NA	NA	NA	17 (5.6%)	NA	183 (60.8%)
Screening using Standard Echocardiography or unspecified echocardiographer												
Selvarani 2014	India	6 months Cross sectional study	Antenatal clinic at a tertiary maternity centre	1125	23.41	NA	NA	NA	NA	NA	NA.	55.73%
Bacha 2019	Ethopia	Cross Sectional Study	Antenatal clinic at tertiary maternity centre	398	27.0 (±4.6)	College/University 49 (12.31%)	8 (2%)	7 (1.8%)	NA	NA	NA	NA
Gomathi 2019	India	4-month cross-sectional study	Cardiology department at tertiary center	300	NA	NA	NA	NA	NA	0	NA	186 (62%)
Bozkaya 2020	Turkey	12-month cross-sectional study	Tertiary delivery center	900	27.4 (±5.8)	NA	0	0	0	0	NA/first trimester	NA
Patel 2021	India	36 month long cross sectional study	Antenatal care at two large hospitals	14275	NA	NA	NA	NA	NA	NA	NA	NA

	CRITERIA USED	RHD ANY n, %	MITRAL REGURGITATION, n (%)	MITRAL STENOSIS (ANY), n (%)	AORTIC REGURGITATION (ANY), n (%)	AORTIC STENOSIS (ANY), n (%)
Studies using Portable or Handlehd Echocardiography						
Otto 2011	WHO consensus statement 2001	Any: 16 (4.6%) Definite: 8 Nondefinite: 8	Any: 12 (3.6%) Mild: 7 Mid/Moderate: 2 Moderate: 2 Moderate/Severe: 1	0	Any: 6 (1.7%) Mild: 6	0
Beaton 2019	WHF	Any: 51 (1.5%) Mild: 31 Moderate: 14 Severe: 6	Any: 45 (1.3%) Mild: 28 Moderate: 15 Severe: 2	Any: 3 (0.1%) Mild: 2 Moderate: 1	Any: 7 (0.2%) Mild: 5 Moderate: 1 Severe: 1	0
Nascimento 2021	Adapted ASE criteria for major heart disease	Any: 12 (1.1%)*	Any: 12 (1.1%) Mild to moderate: 11 Moderate: 1	Any: 1 (0.1%) Mild: 1	Any: 3 (0.3%) Mild: 3	Any: 1 (0.1%) Mild: 1
Snelgrove 2021	WHF	Any: 3 (0.5%)	Any: 1 (0.2%) Moderate: 1	Any: 2 (0.33%) Severe: 2	Any: 1 (0.2%) Moderate: 1	0
AlSharqi 2022	ASE/EACVI recommendations	Any: 20 (6.6%)	'mitral valve involvement': 20 (6.6%)	Significant: 17 (5.6%)	'aortic valve involvement' 3 (1%)	Significant: 1 (0.3%)
Screening using standard echocardiography or nonspecified echocardiographer						
Selvarani 2014	NA	Any: 17 (1.5%)	Any: 1 (0.1%)	Any: 14 (1.2%)	Any: 3 (0.03%)	NA
Bacha 2019	WHF	Significant: 9 (2.3%)	Any: 4 (1%) Moderate to Severe: 2 NS: 2	Moderate to Severe: 3 (0.8%)	Moderate to Severe: 2 (0.5%)	Moderate to Severe: 2(0.5%)
Gomathi 2019	NA	Any: 12 (4.0%)	Any: 4 (1.3%)	Any: 4 (1.3%) Moderate: 3 Not specified: 1	Any: 1 (0.3%) Not specified: 1	Any: 1 (0.3%) Not specified: 1
Bozkaya 2020	WHF	Any: 26 (2.9%)	Any 24 (2.7%) Mild: 20 Moderate: 4	Mild: 2 (0.2%)	0	0
Patel 2021	NA	61 (0.4%)	Any: not specified; 'mitral valve involvement': 61	Number not specified, but '90% were mild to moderate, and 67% had Wilkins score <8'	NA	NA

Table 3 Rheumatic heart disease findings on screening echo.

*RHD on screening was suspected in 36 women (3.2%), but only 56 of the 100 women who screened positive had a confirmatory echocardiogram.

RHEUMATIC HEART DISEASE

Due to high heterogeneity (I^2 > 90%) across the observational studies, data were not pooled, and a narrative description is presented below.

Studies from different global regions were identified, with RHD prevalence ranging from 0.5% in Kenya [28], 1.1% in Brazil [27], 1.5% in Uganda [26], 2.3% in Ethiopia [31], 2.9% in Turkey [33], 4.6% in Eritrea [25] to 6.6% in India [29]. Prevalence of RHD in studies conducted in India varied: Patel et al 0.4% [34], Selvarani et al 1.5% [30], Gomathi et al 2.6% [32] (Figures 2 and 3, and Tables 2 and 3).

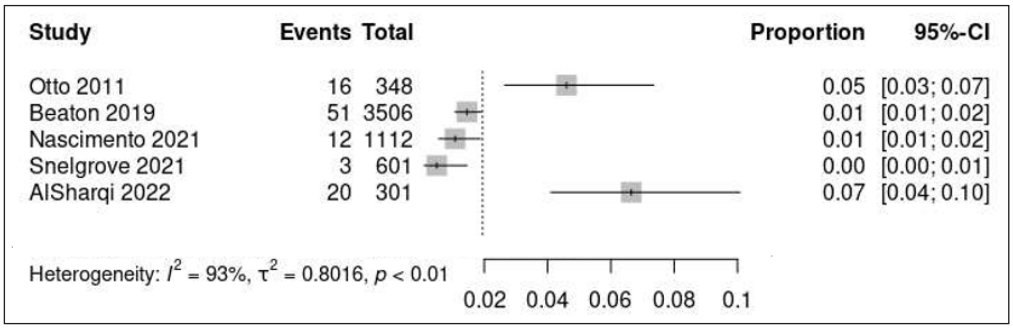

Figure 2 Prevalence of RHD in studies using portable or handheld echocardiography.

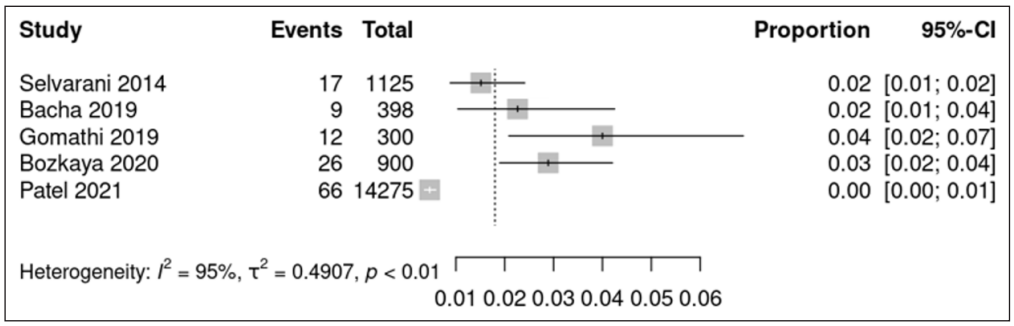

Figure 3 Prevalence of RHD in studies using stationary or non-specified echocardiography.

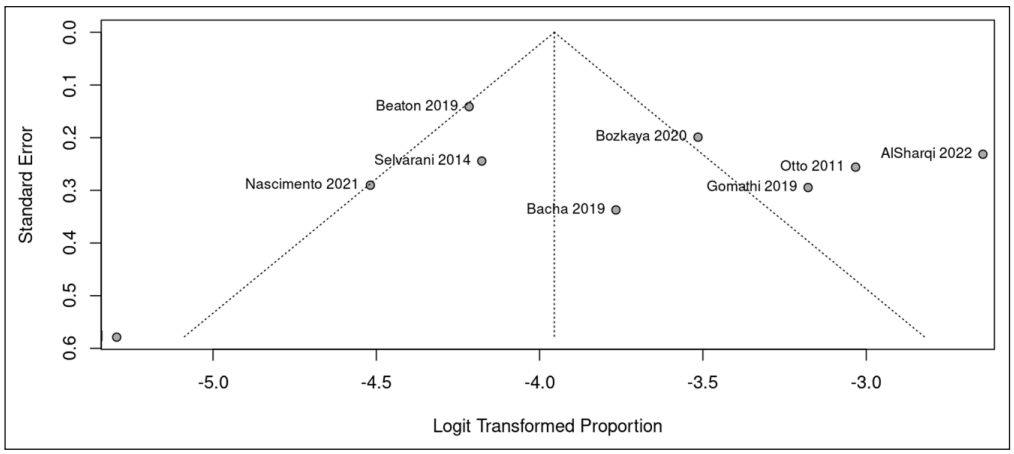

Figure 4 Funnel-plots for assessment of publication bias.

Otto et al. classified their results into three groups, based on pre-defined criteria that predated the 2012 WHF classification (supplementary material – Table S-1) into: definite RHD (n = 8, 2.3%); non-definite RHD (n = 8, 2.3%); and no structural abnormalities. Across the definite and non-definite groups, the mitral valve was the most frequently affected (in 12 of 16 cases). All participants in the study were asymptomatic and none reported known previous RF [25].

Nascimento et al. demonstrated the benefits of portable echo as a screening tool for RHD. Suspected RHD was observed in 36 (3.2%) of 1,112 pregnant women scanned with handheld devices, utilizing a simplified echo protocol [27], and confirmed using more sophisticated portable machines in a smaller subset of women, all with mitral valve involvement and two with additional aortic valve compromise. Prevalence of positive screening findings was comparable in the first (8.9%), second (9.7%) and third (7.2%) trimester [27].

Beaton et al. identified heart disease in 58 women, corresponding to a community prevalence of 1.5% (95% CI 1.3% to 2.1%), with 51 out of 58 cases (87.9%) attributed to RHD [26]. Alsharqi et al., using handheld echocardiography, reported RHD in 20 women (6.6%), all of whom had mitral valve involvement, but no further information was provided regarding the severity of the valvulopathy [29]. Snelgrove et al. identified only 3 cases of RHD (0.5%) [27].

Severe RHD was a rare finding across all studies. Beaton et al. identified 31 women (60.8%) with mild, 14 (24.1%) with moderate, and 6 (11.8%) with severe valvular involvement. Nearly 97% of cases (i.e., all but two) of RHD were new diagnoses. This was the only study providing prospective follow-up of the women diagnosed with RHD during screening, with cardiovascular complications occurred in 51.8% (95% CI 39.0 to 64.3) of these women (heart failure in one third, pulmonary hypertension in one tenth and 5% with arrhythmia), and cardiovascular medication was required in over half [26]. One quarter of the identified women with heart disease were considered either high risk or moderate risk by the combined cardiology/obstetric team. Caesarean delivery was recommended for one woman at the national referral centre, delivery at the regional centre was recommended for seven and six additional women were referred for delivering in hospital [26]. Snelgrove et al. found that none of the three women identified with RHD had a prior formal diagnosis or knowledge of existing CVD disease, despite mitral stenosis being classified as severe in two of the cases [28]. Bozkaya et al. identified mild-to-moderate valve disease in 92.3% of the RHD cases [33]. Patel et al. described the highest number of women with RHD but did not stratify the distribution in any way [34].

OTHER FINDINGS

Among studies using handheld echocardiography, left ventricular systolic dysfunction (LVSD) was an uncommon finding in most of the studies. Two studies reported no cases of LVSD [28, 33] and three reported less than 0.5% prevalence of mild or moderate LVSD [25–27]. The exception was Alsharqi et al., who identified 51 (16.9%) cases of mild/moderate LVSD and 16 (4.7%) cases of severe LVSD from the 301 women imaged [29]. These results were skewed by the inclusion criteria, which comprised a large cohort of women with suspected heart failure (over 50% were NYHA IV at recruitment).

Several studies identified undiagnosed congenital heart diseases in their participants, most commonly intracardiac shunts. Otto et al. and Beaton et al. identified one case each of atrial septal defect [25–26]. Gomathi et al. identified two cases of ASD [32]. Snelgrove et al. detected one case of patent ductus arteriosus, and one case of unroofed coronary sinus [28]. Prevalence in other studies ranged from 1.0% (33), to 2.1% (30) or 2.3% (32) (details in Table 3).

No studies reported on detecting carditis in pregnant participants with clinical presentation compatible with ARF, or time to diagnosis.

QUALITY ASSESSMENT

Study quality varied across studies, with those using portable or handheld echocardiography scoring higher: four out of five studies were judged as low risk and one study [25] was considered medium risk (Table 4). The remaining studies were of lower quality: two were considered low [33] and medium risk [31], all remaining papers were considered high risk [30, 32, 34].

Assessing the three Newcastle-Ottawa scale domains in isolation, all studies but one [32], which was considered high risk, were classified as medium risk for selection bias. Regarding comparability, seven studies were considered low risk [25–29, 31, 33], and 3 were considered high risk [30, 32, 34]. Finally, with respect to outcome, five studies were considered low risk [26–29, 33], and the remaining were medium risk.

Certainty of evidence was considered very low. All studies were observational, and certainty was downgraded on the basis of concerns with risk of bias, inconsistency, imprecision, and publication bias (Figure 4). Justification for the decisions is provided in Table 5.

Table 4 Newcastle Ottawa scale for quality assessment of cross-sectional studies.

Ψ Comparability of subjects across studies with enough information provided on study design, analysis, and confounding factors (**); information provided on 2 of the 3 previously mentioned factors (*).

STUDY ID	SELECTION			COMPARABILITY	OUTCOME		TOTAL	RESULT
	REPRESENTATIVENESS OF THE SAMPLE	SAMPLE SIZE	NON-RESPONDENTS	Ψ	ASSESSMENT OF OUTCOME	STATISTICAL TEST		
Studies using Portable or Handheld Echocardiography								
Otto 2011	*	-	*	**	**	-	6	Medium Risk
Beaton 2019	*	*	-	**	**	*	7	Low Risk
Nascimento 2021	*	*	-	**	**	*	7	Low Risk
Snelgrove 2021	*	*	-	**	**	*	8	Low Risk
AlSharqi 2022	*	-	*	**	**	*	7	Low Risk
Screening using Standard Echocardiography or nonspecified echocardiographer								
Selvarani 2014	-	*	-	*	**	-	4	High Risk
Bacha 2019	*	*	-	**	**	-	6	Medium Risk
Gomathi 2019	-	-	-	-	**	-	2	High Risk
Bozkaya 2020	*	*	-	**	**	*	7	Low Risk
Patel 2021	*	*	-	-	**	-	4	High Risk

NO OF STUDIES	RISK OF BIAS	INCONSIS-TENCY	INDIRECTNESS	IMPRECISION	PUBLICATION BIAS	CERTAINTY
10	Serious	Serious	Low risk	Serious	Serious	⨁◯◯◯ Very low
	5 of 10 studies had medium to high risk of bias as per the Newcastle Ottawa scale	Inconsistency was very high: $I^2 = 95\%$	Study population of pregnant women in high prevalence countries in all studies	The detection rate of RHD was <1% in 2 studies	Asymmetric funnel plot, with Four studies are outside the 95%CI limits	

Table 5 Assessment of Certainty of Evidence using the GRADE approach.

DISCUSSION

Our review shows that screening the antenatal population using handheld or portable echocardiography can identify an important proportion of women with previously undiagnosed RHD living in high-prevalence areas. The observed prevalence varied across the included studies and different global regions. This is not unexpected and may be due to wide variation of RHD prevalence in some geographical areas, as well as the different criteria for diagnosing and reporting RHD across studies. These findings are in-keeping with recent data estimating that the prevalence in countries where RHD remains endemic is >1%, and greatest in women of childbearing ages [7, 34].

A large proportion of the RHD detected was mild in severity, which is generally well tolerated in pregnancy [9]. Although RHD was the most common finding, other clinically relevant conditions, such as congenital heart disease were detected. Some women had LVSD, pulmonary hypertension and high-risk left-sided valve lesions (e.g., aortic valve area <1.5 cm^2, mitral valve area <2 cm^2, or moderate to severe mitral regurgitation), which are included as part of widely accepted risk stratification schemes for women and cardiovascular disease such as CARPREG-II (Table S-2) [35], and the modified WHO classification of maternal cardiovascular risk (Table S-3) [36]. This is of relevance has it shows that besides being important for identifying women in need for secondary antibiotic prophylaxis, echocardiography as part of antenatal screening may be of importance for early detection and planning of pregnancy care in a significant number of women with undetected high-risk cardiovascular conditions living in high-prevalence areas.

The WHO has defined 13 recommendations for maternal and fetal assessment as part of their recommendations for antenatal care (Table S-4 – Supplementary Material) [37]. These include testing for HIV in high prevalence areas, screening for tuberculosis in areas with a prevalence > 1/1000 and an early ultrasound, before 24 weeks of gestation. According to the latest UNAIDS report, prevalence of HIV among adults aged 16 to 45 in Eastern and Southern Africa, and Western and central Africa, was 5.9 and 1.1%, respectively [38]. The early ultrasound may detect fetal anomalies in 1.2% [39], and multiple pregnancies in 1.7% of gestations [40]. These rates are comparable to the prevalence figures we described for RHD screening in our review.

Portable and handheld echocardiography screening may provide a more accessible strategy in these low-income settings where standard stationary transthoracic echocardiography is not easily accessible. There were variations in the strategy used for implementing echocardiography screening the studies we identified. Three studies trained nurses and/or obstetricians for obtaining an echocardiogram, and having the images interpreted remotely by trained cardiologists [26–27, 29]. This strategy seems feasible and therefore might be easier to implement where antenatal care is largely led by community-based clinics, such as in Brazil [27]. Obstetricians, alongside nurses and midwives, perform WHO's recommended antenatal ultrasound in high-prevalence areas for RHD [41] and may constitute potential alternatives upon receival of appropriate training in regions where cardiologists are sparse or lacking.

Timing for echocardiographic screening in pregnancy is still a matter of debate, and further research is needed to address this matter. Earlier screening has the potential advantage of improved acoustic window and adjusting pregnancy management planning in case changes are detected. Data from Beaton et al. provides evidence that antenatal screening with portable echocardiography at median of 24 weeks gestation can impact upon antenatal care and delivery planning [26]. However, we did not identify any studies comparing routine echocardiographic antenatal screening versus standard antenatal care that could provide direct evidence on the impact such an intervention might have upon maternal, fetal, and neonatal outcomes. This is an important knowledge gap that requiring further investigation.

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