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Review Article

Screening methods for congenital anomalies in low and lower-middle income countries: A systematic review

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SUMMARY

Introduction: Surgically correctable congenital anomalies are responsible for a significant burden of morbidity and mortality in children from low-and lower-middle-income countries (LMICs). Early identification through fetal and neonatal screening is critical to reducing death and disability. This study aims to identify feasible screening methods for surgically correctable congenital anomalies in LMICs.
Methods: A systematic search looking at screening for congenital anomalies in LMIC was conducted in seven databases from 2000 until May 25, 2020, with no language restriction. All articles discussing screening methods for surgically correctable congenital anomalies in LMICs were included. Articles were screened by two independent contributors using Rayyan software, with a third contributor resolving conflicts. Feasibility of the screening method and its risk of bias were assessed using the MINORS scale.
Results: Of 3473 articles, 24 were included in the full-text review. Nine screening methods (three prenatal and six postnatal) were identified - the most frequently utilized being physician clinical examination (45.8%), pulse oximetry (33.3%) and fetal ultrasound (20.8%). The use of a birth defect picture toolkit was the most feasible screening method. The risk of bias scale yielded an average of 11.9 points, which corresponds to a moderate level of bias.
Conclusion: Despite clear benefits, prenatal and neonatal screening methods are infrequently used in LMICs to identify surgically correctable congenital anomalies in neonates, likely due to financial, material, and human resource constraints. Further research into the development of low-cost feasible methods is needed within these settings.
Prospero registration number: CRD42020192051.
Type of Study: Systematic review.
Level of Evidence: IV.

1. Introduction

Surgically correctable congenital anomalies contribute to the burden of global pediatric morbidity and mortality [1,2]. Misdiagnosis and non-recognition of surgically correctable congenital anomalies, especially those which are non-visible, lead to delayed referral to adequate care facilities, increasing the associated morbidity and mortality. In Lagos, Nigeria, 42.5% of deliveries occur at commercial traditional maternity homes [3], and 59% of women aged 15–49 years give birth at home supervised by traditional birth attendants (TBAs). While TBAs have the capacity to contribute significantly to maternal and child survival, they are limited in recognizing and managing urgent or serious birth conditions, hence leading to poorer outcomes [4,5].

Identifying existing screening methods will clarify the current prenatal and neonatal screening systems available in low-and lower-middle-income countries (LMICs) and guide future efforts to develop inexpensive, reliable and standardized screening methods for wide dissemination in low-resource settings. The aim of this

Abbreviations: LMICs, low-and lower-middle-income countries; TBAs, traditional birth attendants; MINORS, methodological index for non-randomized studies; MRI, magnetic resonance imaging.

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review is therefore to identify and characterize currently existing fetal and neonatal screening methods used for surgically correctable congenital anomalies in LMICs.

2. Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and checklist for conducting systematic reviews were used [6]. A senior medical librarian searched the following databases from 2000 until May 25, 2020: Medline (Ovid), Embase (Ovid), Cochrane (Wiley), Global Health (Ovid), Web of Science (Clarivate Analytics), Africa Wide Information (Ebsco) and Global Index Medicus (WHO). The search strategy used variations in text words found in the title, abstract or keyword fields, and relevant subject headings to retrieve articles looking at neonatal screening for congenital anomalies in low-income or lower-middle income countries, as defined by the World Bank, with no language restrictions. Animal studies were excluded. The full search strategy can be found in the Supplementary material 1 and the PRISMA-S extension was used for reporting and is included in the Supplementary material 2. The review was registered with the National Institute for Health Research's PROSPERO website (CRD42020192051).

References found were imported into EndNote X9, where duplicates were removed, followed by references being imported into the online platform Rayyan [7] to perform the screening. All titles were screened by two independent contributors (JS, XM) using Rayyan software, with a third contributor (DP) resolving conflicts. The primary reasons for study exclusion can be found in Fig. 1.

The inclusion criteria were articles from 2000 to May 25, 2020; articles in any language; articles discussing prenatal and neonatal screening methods for surgically correctable congenital anomalies and articles in LMICs, as defined by World Bank.

Feasibility of each screening method, defined as its suitability given the available resources, monitoring capacity and acceptable outcomes, was evaluated [8]. The risk of bias of the study was assessed using the Methodological index for non-randomized studies (MINORS) scale [9].

3. Results

The initial search identified 3473 articles, of which 3429 remained following duplicate removal. Following screening, 3382

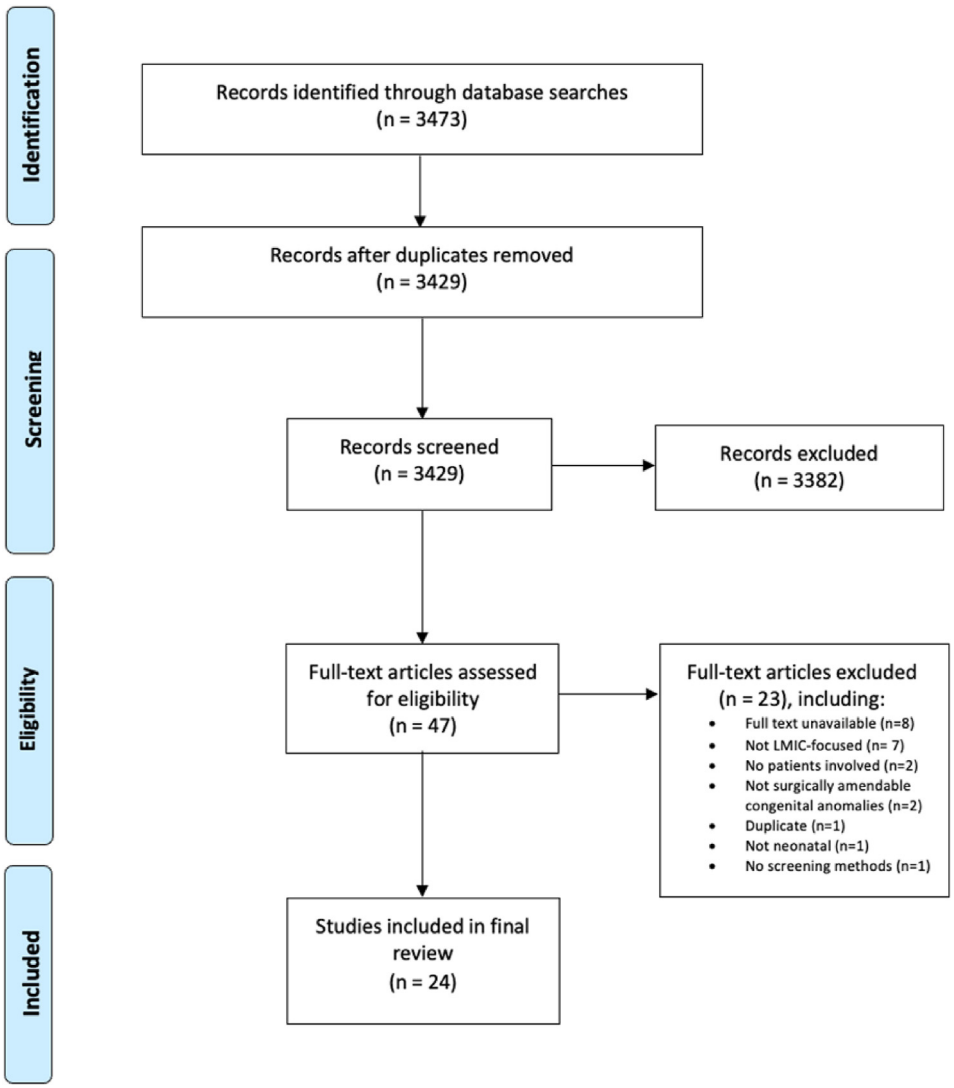

Fig. 1. PRISMA flow diagram.

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Table 1
Summary of the included articles.

Authors (reference)	Year	Type of article	Country	Timing of screening	Screening methods studied	Number of patients	Impact
Mosayebi et al. [10]	2020	Cross-sectional study	Iran	Post-natal	Pulse oximetry	413	Routine pulse oximetry and clinical examinations as screening methods for cardiac and noncardiac diseases in asymptomatic newborns in LMICs.
Vijayaraghavan et al. [11]	2019	Prospective observational study	India	Pre-natal	Fetal echocardiography	240	Prenatal diagnosis and planned peripartum care improved pre-operative status and reduced mortality of neonates with critical congenital cardiac anomalies in LMICs.
Tekleab and Sewnet [12]	2019	Prospective study	Ethiopia	Post-natal	Pulse oximetry	941	Pulse oximetry screening for critical congenital heart disease may yield a high rate of false positives in high altitudes however it is useful in detecting non-cardiac causes of hypoxemia.
Rakha and El Marsafawy [13]	2019	Retrospective study	Egypt	Pre-natal	Fetal echocardiography	458	Fetal echocardiography is a highly sensitive and specific tool for prenatal detection of congenital heart disease in high-risk pregnancies in developing countries
Mumpe-Mwanja et al. [14]	2019	Prospective study	Uganda	Post-natal	Clinical examination (photo)	69,766	Epidemiological data on congenital anomalies can be obtained through hospital-based surveillance in order to inform prevention policies and service provision needs in LMICs.
Mohsin et al. [15]	2019	Prospective study	Pakistan	Post-natal	Pulse oximetry, clinical examination (physician)	1650	Using both pulse oximetry and clinical examination as screening tools for congenital heart anomalies is more efficient than one method alone in a community health setting in LMICS.
Mohan et al. [16]	2019	Retrospective study	India	Pre-natal	Fetal MRI	330	MRI complements fetal ultrasound in the prenatal evaluation of fetal anomalies
Kamla et al. [17]	2019	Prospective multicenter cohort study	Cameroon	Post-natal, Pre-natal	Clinical examination (physician), fetal ultrasound	21,113	Prenatal screening and diagnosis of congenital anomalies is very important and national registries of visible congenital anomalies should be created
Onyambu and Tharamba [18]	2018	Descriptive cross-sectional study	Kenya	Pre-natal	Fetal ultrasound	500	Fetal Screening for congenital anomalies using ultrasound should be an important component of primary health care for maternal and child health
Ekwochi et al. [19]	2018	Prospective study	Nigeria	Post-natal	Clinical examination (physician)	90	Birth weight, maternal socio-economic class, maternal educational level, parity, febrile illness and the use of traditional medicine are important risk factors associated with congenital anomalies.
Akinmoladun et al. [20]	2018	Prospective study	Nigeria	Pre-natal	Fetal ultrasound	989	In LMICs early identification of congenital anomalies will help in proper management and decrease morbidity and mortality.
Shahzad et al. [21]	2017	Cross-sectional study	Pakistan	Post-natal	Pulse oximetry, echocardiography	138	Use of pulse oximetry to screen for critical congenital heart anomalies in

(*continued on next page*)

Table 1 (*continued*)

Authors (reference)	Year	Type of article	Country	Timing of screening	Screening methods studied	Number of patients	Impact
							neonates is effective in a low-resource setting.
Sharma et al. [22]	2017	Prospective study	India	Pre-natal	Fetal echocardiography	1200	Fetal echocardiography should be an integral part of all second trimester anomaly scans
Tchente Nguefack et al. [23]	2015	Cross-sectional study	Cameroon	Pre-natal, Post-natal	Fetal ultrasound, clinical examination (physician)	6048	Early detection of congenital anomalies prenatally will facilitate appropriate management
Forum Shah et al. [24]	2015	Prospective longitudinal study	India	Post-natal	Pulse oximetry, clinical examination (physician), echocardiography	700	Pulse oximetry is an useful routine screening tool for neonates with critical congenital heart diseases in rural communities.
Emdin et al. [25]	2015	Cross-sectional study	Pakistan	Post-natal	Pulse oximetry, clinical examination (physician)	353	Pulse oximetry is feasible for routine screening of neonates in primary care in LMICs.
Mathur et al. [26]	2015	Prospective study	India	Post-natal	Pulse oximetry, clinical examination (physician)	945	Neonates with cyanotic heart diseases can be effectively screened using pulse oximetry.
Hoang et al. [27]	2013	Prospective study	Vietnam	Post-natal	Clinical examination (photo)	13,954	Data from population-based studies on external birth defects may be useful in setting up birth defects registries
Agunloye et al. [28]	2011	Longitudinal study	Nigeria	Post-natal	Post-natal ultrasound	202	In low-resource settings, neonatal ultrasound scans are useful in detecting prenatally missed congenital anomalies.
Vaidyanathan et al. [29]	2011	Prospective study	India	Post-natal	Pulse oximetry, clinical examination (physician), echocardiography	5487	Pulse oximetry and clinical evaluation had very low sensitivity for screening for congenital heart anomalies in neonates in a community setting in a LMIC.
Eshete et al. [30]	2011	Cross sectional study	Ethiopia	Post-natal	Clinical examination (non-physician)	42,986	Routine clinical examination identifies surgically correctable congenital anomalies.
Saha et al. [31]	2009	Prospective study	India	Pre-natal	Fetal ultrasound	6682	Prenatal screening helps determine incidence of congenital anomalies and management of the disease postnatally.
Bakare et al. [32]	2009	Prospective study	Nigeria	Post-natal	Clinical examination (physician)	624	Congenital anomalies screening revealed ethnic variations in incidence of birth defects.
Patel and Adhia [33]	2005	Prospective study	India	Post-natal	Clinical examination (physician)	17,653	Congenital anomalies need to be identified early so that proper management can be instituted.

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articles were excluded. 47 full text articles were assessed for eligibility and 24 articles were included in the final review [10–35] (Fig. 1, Table 1). The included articles originated in 13 different countries in Asia, Africa and the Eastern Mediterranean region, with 4 studies from India, 4 from Pakistan and 3 from Nigeria (Fig. 2). Sixteen (66.7%) studies were prospective, 6 (25%) cross-sectional, and 2 (8.3%) retrospective. Fifteen (62.5%) articles explored a single screening method, 7 (29.2%) addressed two methods, and 2 (8.3%) addressed 3. Overall, 9 different screening methods (3 antenatal and 6 postnatal) were discussed in the included articles (Fig. 3). The anomalies most screened for were cardiac, followed by urological, general surgical and neurosurgical anomalies (Fig. 4) The impact of screening methods is summarized in Table 1.

Antenatal screening methods were used in 9 (37.5%) articles, including fetuses between 18 and 37 weeks gestational age. Urological congenital anomalies were the most targeted in prenatal screening procedures, followed by cardiac, general surgery and neurosurgical anomalies (Fig. 4). The most commonly studied method was fetal ultrasound (n = 5, 55.6%), followed by fetal echocardiography (n = 3, 33.3%) and magnetic resonance imaging (MRI) (n = 1, 11.1%). Antenatal screening using ultrasound scan,

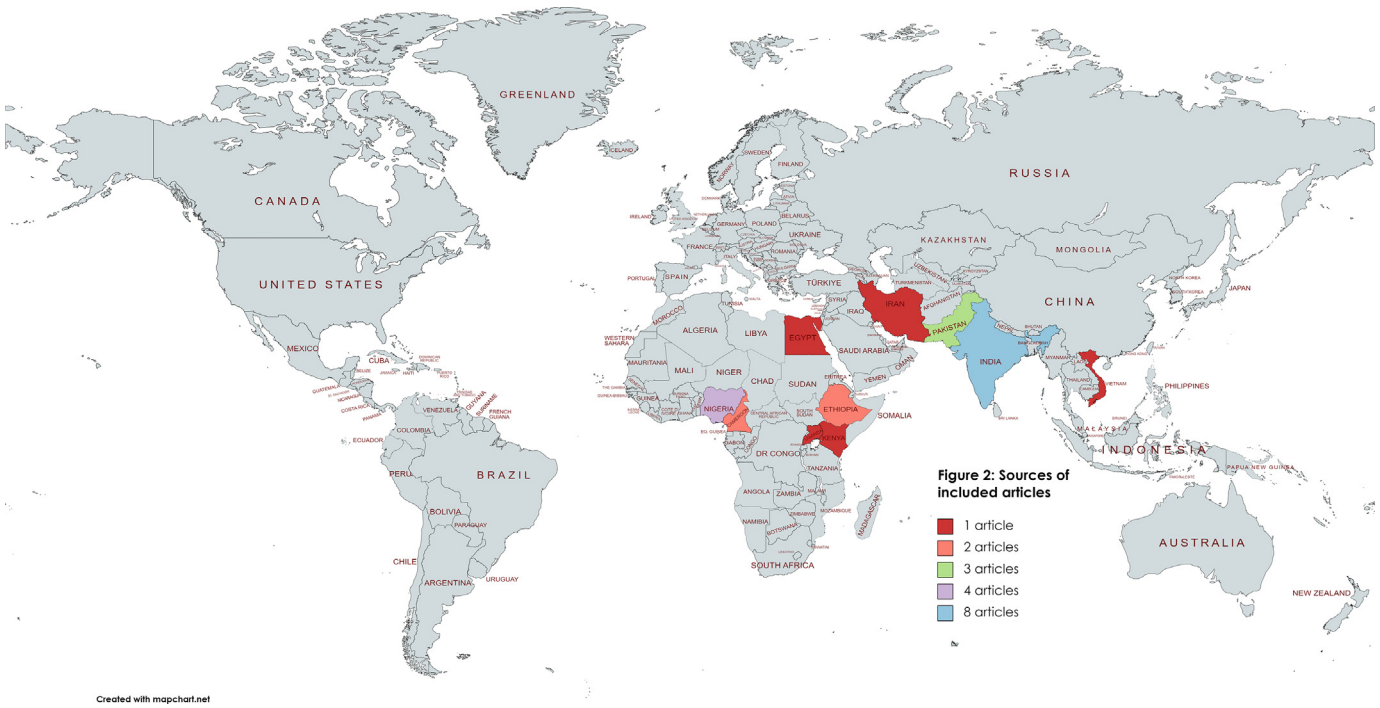

Fig. 2. Countries of origin of included articles.

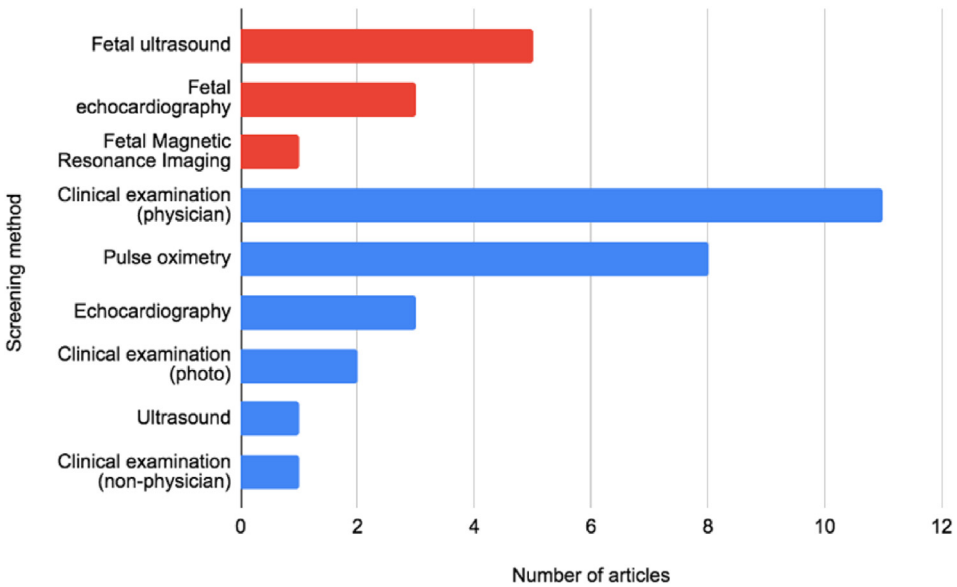

Fig. 3. Frequency of screening methods discussed in the included articles (antenatal = red, postnatal = blue). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

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successfully diagnosed fetal anomalies and was useful in facilitating counseling and prenatal intervention, ensuring appropriate postnatal management and ultimately decreased morbidity and mortality [18,20] The prevalence of congenital anomalies using ultrasound was 1.64% [23], while the antenatal detection rate was 21% for visible congenital anomalies [17]. This low detection rate was attributed to insufficient number of antenatal scans performed and lack of expertise of scanning personnel in making diagnoses. In one study, 77.1% of the babies with abnormal antenatal renal scan had renal tract malformations postnatally [31]. MRI was found to complement ultrasound in the evaluation of fetal anomalies and provide additional information on select cases before 20 weeks [16]. Fetal echocardiography was specific to the detection of cardiac anomalies, with a 97.0% sensitivity, 99.1% specificity, and 98.47% accuracy [13].

Seventeen articles (70.1%) focused on postnatal screening methods, applicable to infants from 1 h to 59 days of age, with 50% of the articles targeting neonates less than 24 h of age. Clinical examination by a physician (n = 11, 42.3%), pulse oximetry (n = 8, 30.8%) and echocardiography (n = 3, 11.5%) were the most frequently used methods (Fig. 6). Congenital anomalies most screened for postnatally were cardiac anomalies, followed by urological, general surgical and neurosurgical anomalies (Fig. 6). Using clinical evaluation in a hospital-based surveillance project to generate reliable epidemiologic data, the prevalence of birth defects was 65–67 per 10,000 live births [14,19]. The incidence of congenital anomalies based on clinical examination was reported to be 6.9% in Nigeria [32] and 9.6% in India [33]. Using a combination of clinical evaluation and photographs, one study reported an incidence of visible birth defects of 6 per 1000 [27], and in Ethiopia, cleft lip and palate were found to be endemic by trained midwives performing newborn clinical examination [30].

Clinical evaluation had 92% sensitivity and 98.6% specificity for the detection of congenital heart disease [15] and a 95.2% sensitivity and 52.4% specificity for cyanotic heart disease [26]. Pulse oximetry without clinical evaluation varied between a 32% and 76.2% sensitivity and 99.5% and 83.7% specificity for congenital heart disease detection [15,21]. Although, when combined, clinical evaluation and pulse oximetry improves the detection rate one study reported sensitivity of 19% for all congenital heart diseases and 20% for major congenital heart diseases and specificity of 88% [29]. Screening congenital cardiac disease using pulse oximetry and clinical evaluation is feasible and acceptable to parents. Echocardiography was used to confirm diagnosis in individuals with positive screening results from clinical evaluation and pulse oximetry [29].

The feasibility analysis of the included screening methods in the LMIC context identified 3 feasible methods: clinical examination of the newborn using pictures, clinical examination by non-physician, and ultrasound (Fig. 5). Three other methods (clinical examination by a physician, fetal ultrasound and pulse oximetry) were deemed somewhat feasible, while the rest of the methods were deemed unrealistic given the specific setting.

A risk of bias assessment performed using the MINORS scale resulted in a score of 11.9 out of16, corresponding to a moderate level of bias (Fig. 6). Included articles scored best in terms of “inclusion of consecutive patients” and “prospective collection of data”. Meanwhile, they scored poorly in the categories “unbiased assessment of the study endpoint” and “prospective calculation of the study size”, with 19 and 14 articles, respectively, scoring 0.

4. Discussion

Early identification of surgically correctable congenital anomalies allows for proper management and planning of intervention with resultant improved outcomes. Although newborn screening programs are well established in most high-income countries, these birth defects screening and surveillance programs are missing, or have only recently been developed in LMICs. In these regions which have the highest number of birth defects (94% of all defects and 95% of associated deaths) multiple challenges in terms of resources, training and sustainability of the surveillance programmes exist [17]. Inexpensive screening methods for surgically correctable congenital anomalies in neonates are however available for use in LMICs and combining multiple screening methods can increase recognition and diagnosis of these conditions while significantly reducing delays in management. The studies included did not however offer any evidence of concerted efforts in establishing systematic programs in LMICs targeted at identifying surgically treatable congenital anomalies on the level, scale and dimension it exists for non-surgical congenital conditions. In all the articles reviewed, invasive screening tests for prenatal diagnosis were not deployed. This buttresses the need for screening methods

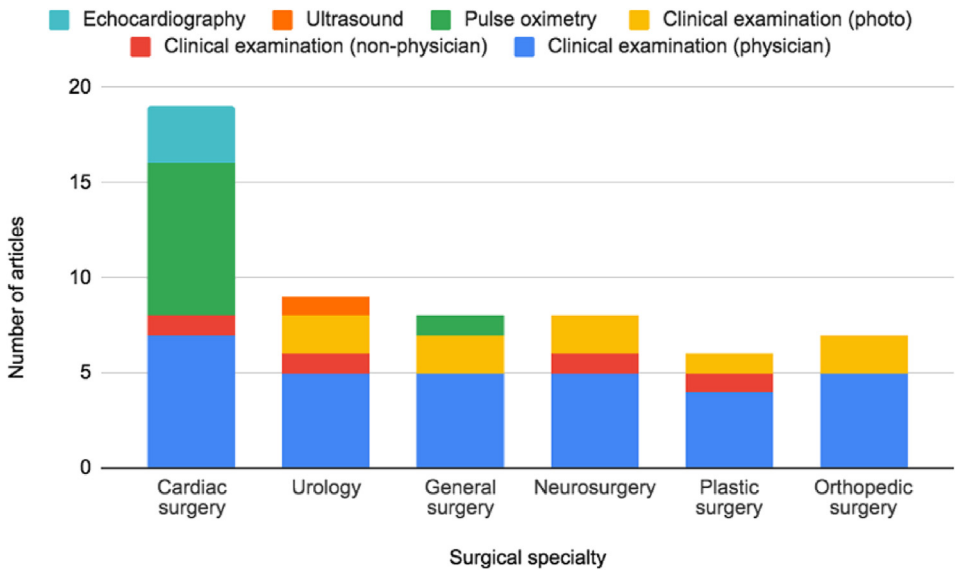

Fig. 4. Number of articles by screening method and specialty.

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Type of screening method	Easy-to-use	Easy to maintain	Scalability	Available support	Easy to train local workers	Efficient (sensitivity)	Low-cost or cost-effective	Reusable	Number of articles	Average score	Conclusion
Fetal echocardiography									3	-3	Not feasible
Fetal ultrasound									5	1.4	Somewhat feasible
Fetal Magnetic Resonance Imaging									1	0	Not feasible
Clinical examination (physician)									11	2.73	Somewhat feasible
Clinical examination (non-physician)									1	-2	Feasible
Clinical examination (photo)									2	5	Feasible
Pulse oximetry									8	0.25	Somewhat feasible
Ultrasound									1	0	Feasible
Echocardiography									3	-2.67	Not feasible

Fig. 5. Feasibility assessment of each screening method based on principles developed by Cook and Ellaway [35].

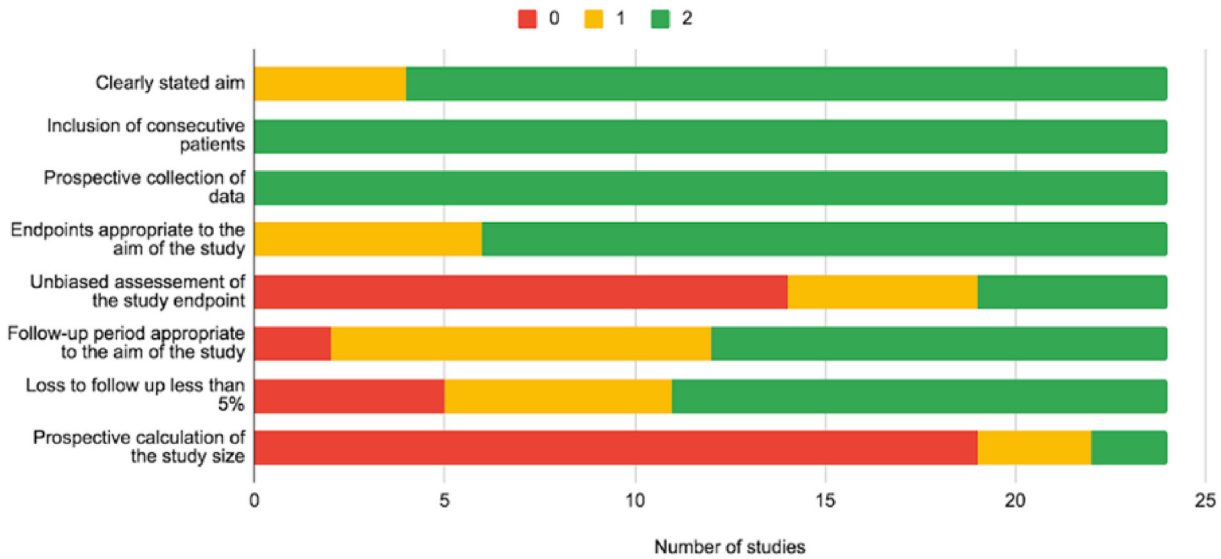

Fig. 6. Risk of bias assessment with the MINORS scale for non-randomized studies [9].

in LMICs to be easily accessible, inexpensive, and not require high technical skills.

The studies reviewed were quite heterogeneous in nature and limited in geographical coverage, with more than a third of the articles focusing only on screening for congenital cardiac anomalies, and one third originating from 2 Asian countries. Early identification and treatment of other relatively common congenital anomalies such as anorectal malformations, intestinal atresias, esophageal atresias, posterior urethral valves and club foot deformities, to mention just a few, can greatly impact outcome and improve the quality of life of affected children. Late identification, diagnosis and treatment result in increased morbidity and mortality and reduced quality of life. Specific screening for these other highly relevant congenital anomalies were not evaluated in any of the articles reviewed.

Clinical evaluation with or without adjunct screening tools was used in more than 40% of the studies and across all the surgical specialties interrogated. Clinical evaluation by physicians with or without the picture portfolio ranked highest on the feasibility assessment. This has important implications for the development of any comprehensive screening tool and method for this region.

Fetal ultrasound scan is a somewhat feasible screening tool, which allows early identification of congenital anomalies and proper planning of perinatal care and interventions. It has been suggested that fetal ultrasound screening be made an integral part of primary health care with the inclusion of fetal echocardiography as a component of second trimester prenatal scans [22]. The addition of prenatal ultrasound screening to antenatal care in LMICs has been shown to improve prenatal detection, helping to reduce morbidity and mortality and improving the clinical decision-making process [23]. One remaining challenge however is the late commencement of antenatal care by mothers in the region, and the large cohort of women receiving obstetric care outside of hospitals. The successful use of midwives in the surveillance of congenital anomalies using clinical evaluation and photographs may imply that a model could be created that incorporates TBAs in settings where most births occur out of hospital, for a more

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comprehensive coverage [14]. This would require in-depth training or the use of other personnel as surveillance officers. As most current congenital anomalies screening reports are based on hospital data, inclusion of TBAs and other surveillance officers will allow investigators to obtain more accurate population-based data. Based on our literature review, we can suggest the following components as part of a population-based congenital anomalies screening program: clinical examination with photographs for accurate identification, pulse oximetry and prenatal ultrasound.

5. Limitations

As our review was limited to low and lower-middle income countries, we may have missed some screening methods used in middle-income countries that could have shed some light on similar issues. Another limitation is the heterogeneity of articles, as well as the lower quality of some papers, as identified by our risk of bias assessment.

6. Conclusion

Screening for surgically correctable congenital anomalies in LMICs is feasible with various screening methods demonstrating high specificity, sensitivity and accuracy. A comprehensive, reliable and inexpensive tool needs to be created to facilitate early diagnosis in LMICs. This will help to improve the current late presentations and poor outcomes from these conditions.

Funding source

None.

Declaration of competing interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpedsurg.2023.01.038.

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