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SYSTEMATIC REVIEW

Trends in Ultrasound Use in Low and Middle Income Countries: A Systematic Review

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ABSTRACT

Background: Evidence on recent trends regarding the impact and cost-benefits of ultrasound in resource-constrained settings is limited. This study presents a systematic review to determine recent trends in the utility and applicability of ultrasound use in low and middle income countries (LMIC). The review includes characterizing and evaluating trends in (1) the geographic and specialty specific use of ultrasound in LMICs, (2) the innovative applications and the accompanying research findings, and (3) the development of associated educational and training programs.

Methods: The electronic databases Medline OVID, EMBASE, and Cochrane were searched from 2010 to 2018 for studies available in English, French, and Spanish. Commentaries, opinion articles, reviews and book chapters were excluded. Two categories were created, one for reported applications of ultrasound use in LMICs and another for novel ultrasound studies.

Results: A total of 6,276 articles were identified and screened, 4,563 studies were included for final review. 287 studies contained original or novel applications of ultrasound use in LMICs. Nearly 70% of studies involved ultrasound usage originating from Southeast Asia and sub-Saharan Africa, the latter being the region with the highest number of innovative ultrasound use. Educational studies, global collaborations, and funded studies were a substantial subset of overall ultrasound research. Our findings are limited by the lack of higher quality evidence and limited number of randomized clinical trials reported.

Conclusion/Global Health Implications: Our systematic literature review of ultrasound use in LMICs demonstrates the growing utilization of this relatively low-cost, portable imaging technology in low resource settings.

Key words: • Ultrasound • Ultrasonography • Echocardiogram • LMIC • Low resource • Global health • Systematic review

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1. Introduction

Ultrasonography is a clinically accepted imaging modality that enables a low-powered, mobile diagnostic pathway that can be readily learned by a variety of medical personnel to enable rapid assessment and treatment in a variety of settings. Ultrasonography devices are able to be used by a single-operator, handheld, and can provide diagnostic capabilities at a much lower cost than other imaging tools such as Computed Tomography (CT) or Magnetic Resonance Imaging (MRI). These characteristics make ultrasonography (otherwise referred to as ultrasound (US)) an attractive option for clinical use in low and middle income countries (LMICs) for both in-patient and out-patient use.

In 1997, the World Health Organization (WHO) estimated that 50% of the developing world did not have access to ultrasound imaging, and where it was available, equipment was outdated or broken.¹ Technically trained maintenance for machine repair and the circulation of unregulated ultrasound equipment presented barriers to imaging access in metropolitan areas, in addition to the substantial lack of access to healthcare and imaging resources in rural areas. However, recognition of the potential advantages of ultrasound imaging in low resource settings has spurred the growth of ultrasound machine availability, diagnostic capability, trained technologists, educational and training programs, research and overall ultrasound utilization in LMICs.²

Despite this progress, there has been little recent literature on the applications of ultrasound in LMICs, including new uses for diagnosis and treatment adapted for medical challenges in low resource settings. We conducted a systematic review to determine recent trends in the utility and applicability of ultrasound use in LMICs. We aim to characterize and evaluate trends in (1) the geographic and specialty specific use of ultrasound in LMICs, (2) the novel applications of ultrasound imaging in low-resource settings and the accompanying research findings, and (3) the development of educational and training programs adapted for ultrasound use in LMICs.

2. Methods

We performed a systematic review of the literature with search strategy development assistance by a trained medical librarian (LO) at Baylor College of Medicine. Medline OVID, EMBASE, and Cochrane Clinical Trials were searched with the developed strategy for English, Spanish and French articles from 2010 to 2018. Low and middle income countries were selected by the World Bank definition and categorization in the year 2018; countries with low income economies and lower-middle economies were chosen for inclusion. Commentaries, opinion articles, reviews and book chapters were excluded. The last search was completed on April 4th, 2019.

Two categories for study selection were created; (1) 'applications of ultrasound,' or all studies using ultrasound imaging technology in a medical context, and a sub-category, (2) 'novel ultrasound research.' Novel ultrasound research studies were selected from articles included in the first category, and were defined as involving *novel application* of ultrasound technology in a low resource setting, involving the use of a hand-held ultrasound probe, or including educational and training curriculum on ultrasound imaging in a low resource setting. For example, "Simplified rheumatic heart disease screening criteria for handheld echocardiography" was included as a novel study, but "Prevalence of rheumatic heart disease in Zambian school children" was not included as a novel study. Both were included in the systematic review of all ultrasound studies in LMICs.

Study selection was performed independently by three researchers (SN, GT and SK), discrepancies between reviewers were resolved by KS. Data extraction was performed using a standardized template by five researchers (SN, SL, GT, SK and RP) and reviewed by KS.

Data collected on all ultrasound studies include the year of publication, journal title, article title, country, and geographical region. Data collected on novel ultrasound studies include (in addition to the above) the hospital type (public vs. private), institution type (tertiary, district or primary care health center), study design, name of first and last author, institution of first and last author, and country of first and last

author, application of ultrasound, medical specialty, type of ultrasound machine, skill level of provider, title of provider, descriptive findings of the study, and study outcomes (depending on study design). Novel ultrasound research articles that were randomized controlled trials were reviewed and graded according to the Cochrane Risk of Bias Tool.³ Data was aggregated and analyzed in Excel (Microsoft, Redmond, WA, USA). Statistical analysis was performed in SPSS (V.21, IBM, Armonk, NY, USA).

This study was exempt from institutional review board approval. The review protocol has not been previously published or registered. We completed

our review following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

3. Results

Initial database search (after deduplication) yielded 6,276 articles (Figure 1). Abstracts were reviewed for inclusion, after which 1,713 studies were excluded for not reporting ultrasound use, describing non-clinical applications, or for studies not performed in an LMIC. An additional 287 articles were included in the novel research sub-category as defined above. Nine articles that met novel research

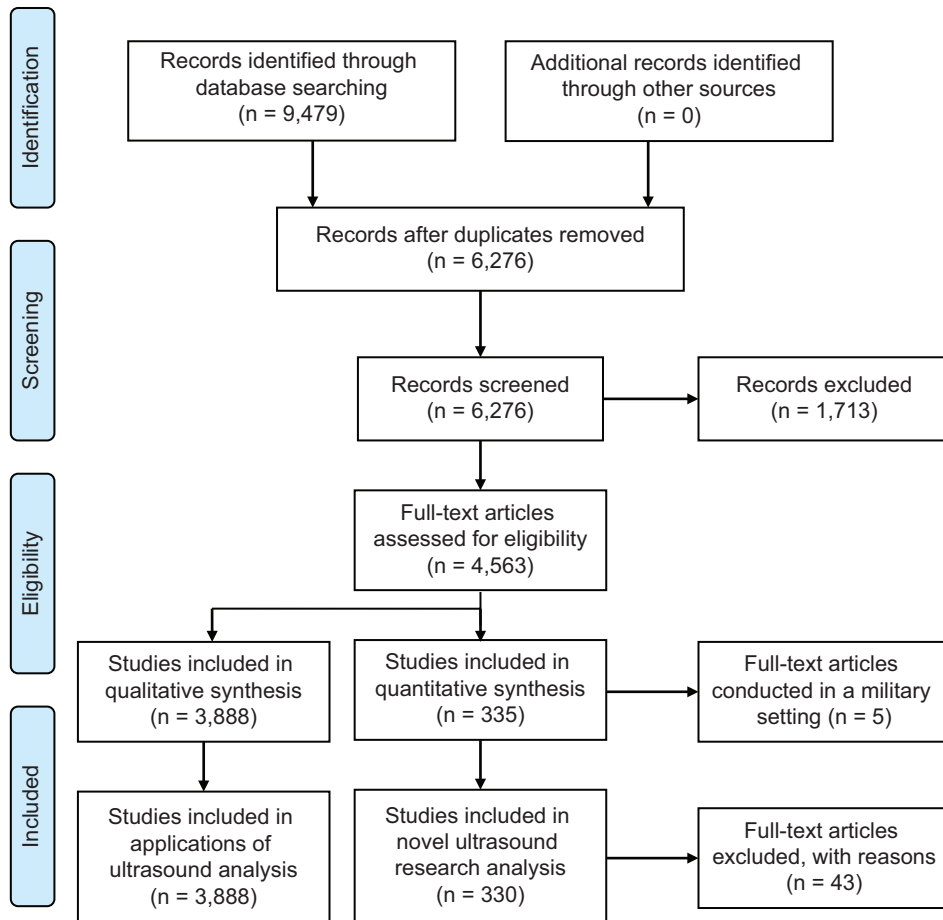


Figure 1: PRISMA flow diagram

Novel: designates novel ultrasound research studies (n=287); Application: designates all applications of ultrasound studies included in review (n=3,888)

criteria were excluded after the full-text was not available for review, with an additional 5 articles excluded for being research studies conducted in a military setting.

Trends by year and geographical region of ultrasound use in LMICs for all studies and novel ultrasound studies are shown in Figures 2 and 3. The number of countries with reported ultrasound use has increased 24% since 2010 from 50 to 62 countries. The countries with the highest number of ultrasound studies included India (20%), Egypt (9.8%), Nigeria (8.8%), and Pakistan (7.3%). The specialties

represented in all ultrasound studies included cardiology (25%), obstetrics and gynecology (14%). Other key specialties included gastroenterology (7.3%), pediatrics (5.8%), infectious disease (5.7%), internal medicine (6.2%), endocrinology (2.9%), and general surgery (3.5%). The most common journals of publication were the Indian Heart Journal (n=103), the Pan African Medical Journal (n=77), the Journal of Medical Case Reports (n=57), Mymensingh Medical Journal (n=53), Pakistan Journal of Medical Sciences (n=50), PLoS ONE (n=48), and BMC Research (n=44).

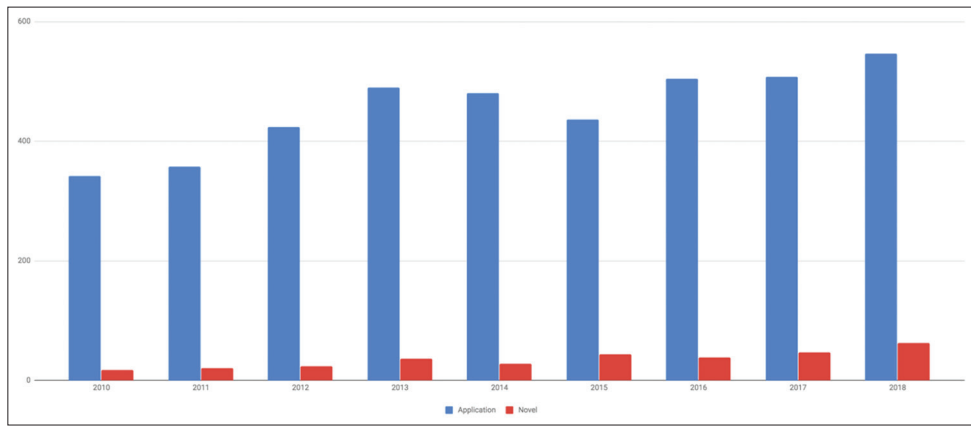


Figure 2: Ultrasound studies in LMIC over time
 Novel: designates novel ultrasound research studies; Application: designates all applications of ultrasound studies included in review

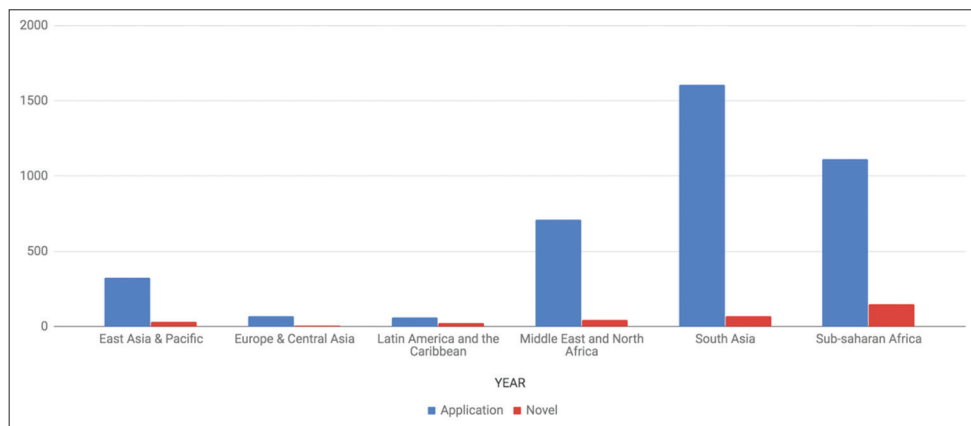


Figure 3: Ultrasound studies in LMIC by geographical region
 Novel: designates novel usage of ultrasound studies; Application: designates all non-novel application of ultrasound studies included in review

Of the 287 novel ultrasound application studies, 48% were prospective studies, 13% qualitative, 12% retrospective, 11% cross-sectional studies, 8% case reports, 5% randomized controlled trials, and 1.0% case-controls. Studies were largely performed at public hospitals (86%), of which 59% were conducted at tertiary hospitals and 41% were carried out in a primary care or rural setting. Novel research studies in the form of RCTs are shown in Table 1.

The novel applications of ultrasound technology in novel studies was primarily for screening (26%) and obstetrical use (34%), however, key applications also included infectious disease (10%), cardiology (9%), abdominal conditions (8%), trauma (8%), and gynecologic conditions (3%). Ultrasound imaging providers in novel studies included physicians (85%), midwives (7%), residents (3%), community health workers (2%), and ultrasound technicians (2%). Hand-held ultrasound devices were used in 28% (n=47) of novel studies. The most common journals of publication for novel ultrasound research include the Journal of Ultrasound in Medicine (n=12), BMC Pregnancy and Childbirth (n=7), Critical Ultrasound Research (n=7), PLoS ONE (n=6), Egyptian Journal of Radiology and Nuclear Medicine (n=5), the Egyptian Journal of Chest Diseases and Tuberculosis (n=5), and the American Journal of Tropical Medicine and Hygiene (n=5).

Global collaboration, defined as the inclusion of at least one author whose listed publication affiliation was within the country in which the novel ultrasound study was conducted, was present in 70% of studies. The majority of studies that involved global collaboration occurred in India (n=22), Uganda (n=22), Nigeria (n=15) and Tanzania (n=15). Of first authors, 67% were from the country of ultrasound study, of last authors, 60% were from the country of ultrasound study. A total of 75 papers (26%) included both a first and last author from the country of ultrasound study, including 18 from India and 14 from Nigeria. Thirty one percent of novel ultrasound research was funded (n=91), including by NIH grants, the Bill and Melinda Gates Foundation, the General Electric (GE) Foundation, and European foundation grant funding. The countries with the most number of studies with funding were Uganda (n=13), Tanzania (n=10), and Rwanda (n=6). Using the Cochrane

risk of bias tool, 70% of the studies reviewed were characterized of having more than one categorized medium and high risk of bias for at least one 'Risk of Bias' category.

Sixty eight percent of novel research studies (n=196) contained an educational or training component on ultrasound imaging. Of those educational studies, 91 (46.4%) occurred in the sub-Saharan geographical region, including a majority in Uganda (n=20), Nigeria (17), and Tanzania (n=9). Details of educational studies with funding and known ultrasound, including a description of the training program or curriculum, are shown in Table 2. The number of annual educational ultrasound studies has increased to nearly 2.9 times the amount from 2010 to 2018 (from 14 to 40 per year).

4. Discussion

Increasing Use of Ultrasound

Our systematic literature review of ultrasound use in LMICs demonstrates the growing utilization of this relatively low-cost, portable imaging technology in low resource settings. Although the WHO does not measure access to ultrasound alongside other imaging modalities such as CT and MRI, it does recognize the importance of ultrasound imaging and its potential impact on diagnostics worldwide.⁴ This includes a goal of meeting 90% of imaging needs in primary health care settings with the use of a general purpose ultrasound machine combined with an X-ray unit, along with distribution of the WHO published Manual of Diagnostic Ultrasound.⁵ Our study demonstrates that research studies regarding ultrasound use in LMICs have increased nearly 60% and expanded 20% geographically in the last ten years in efforts to meet those goals. However, evidence also suggests that the majority of ultrasound studies were conducted at tertiary care centers (more than 70% of all ultrasound studies) and within middle-income countries, demonstrating broader problems with lack of access to healthcare in low-income economies and especially in rural areas.

Regional Trends of Ultrasound

Examining the regional breakdown of ultrasound related studies in LMICs, our study determined

Table 1: Novel randomized controlled trial ultrasound studies in LMICs

First Author	Year	Title	Journal	Country	N	Outcome measured	Outcome Field	Ultrasound used
Abdelhamid ¹	2013	Ultrasound-guided intrathecal anesthesia: Does scanning help?	Egyptian J J of Anaesthesia	Egypt	90	Rate of successful placements with US vs non-US placements	Anesthesia	Sonosite S-Nerve
Akudu ²²	2018	Ultrasonographic study of the incidence of pyramidal lobe and agenesis of the thyroid isthmus in Nnewi population	Journal of Ultrasonography	Nigeria	321	Rate of abnormal thyroids screened	Internal Medicine	Siemens Sonoline Prima
Ansa ²³	2013	The clinical utility of echocardiography as a cardiological diagnostic tool in poor resource settings	Nigerian Journal of Clinical Practice	Nigeria	244	Percent of echocardiography confirmation of suspected heart abnormalities	Cardiology	ALOKA SSD 4000
Barda ²⁴	2017	Ultrasonographic evaluation of urinary tract morbidity in school-aged and preschool-aged children infected with S. haematobium and its evolution after praziquantel treatment: A RCT	PLoS Neglected Tropical Diseases	Cote d'Ivoire	250	Percent of pre-school aged and school aged children positive for S. haematobium at follow-up	Internal Medicine	Sonosite I80 Plus
Beaton ²⁵	2015	The utility of handheld echocardiography for early rheumatic heart disease diagnosis: a field study	Eur Heart J Cardiovasc Imaging	Uganda	4773	HAND Echo relative sensitivity / specificity for RHD detection	Cardiology	GEVivid-i; GEVscan
Beaton ²⁶	2014	The utility of handheld echocardiography for early diagnosis of rheumatic heart disease	J Am Soc Echocardiogr	Uganda	125	HAND Echo ability to distinguish normal patients vs those with RHD sensitivity and specificity	Cardiology	GEVivid-i; GEVscan

(Contd...)

Table 1: (Continued)

First Author	Year	Title	Journal	Country	N	Outcome measured	Outcome Field	Ultrasound used
Bhavnani ²⁷	2018	A Randomized Trial of Pocket Echo Integrated Mobile Health Device Assessments in Modern Structural Heart Disease Clinics	JACC Cardiovascular Imaging	India	253	Percentage reduction in risk of hospitalization and/or death	Internal Medicine	GEVScan
Cherniak ²⁸	2017	Effectiveness of advertising availability of prenatal ultrasound on uptake of antenatal care in rural Uganda: A cluster randomized trial	PLoS ONE	Uganda	157	The number of women receiving antenatal treatment in advertised arm vs non-advertised arm	Obstetrics & Gynecology	Portable - not specified
Choi ²⁹	2011	Interpretation of remotely downloaded pocket-size cardiac ultrasound images on a web-enabled smartphone: Validation against workstation evaluation.	Journal of the American Society of Echocardiography	Honduras	89	Intraobserver agreement comparing interpretations on workstations and smartphones	Cardiology	GEVscan
Goldenberg ³⁰	2018	Routine antenatal ultrasound in low- and middle-income countries: first look - a cluster randomised trial	BJOG	DRC / Guatemala / Kenya / Pakistan / Zambia	49,001	Relative risk composite outcome in US study vs non-US study population	Obstetrics & Gynecology	GE Healthcare - not specified
Greenwood ³¹	2014	Implementing an obstetric ultrasound training program in rural Africa	Int. J. Gynaecol. Obstet.	Mozambique	1,734	Percentage of scans with a clinical impact	Obstetrics & Gynecology	M-Turbo (Sonosite, Bothell, WA, USA) portable ultrasound

(Contd...)

Table 1: (Continued)

First Author	Year	Title	Journal	Country	N	Outcome measured	Outcome Field	Ultrasound used
McClure ³²	2014	First look: a cluster-randomized trial of ultrasound to improve pregnancy outcomes in low income country settings	BMC Pregnancy & Childbirth	Multiple	TBD	TBD - underway	TBD - underway	Obstetrics & Gynecology NA
Nathan ³³	2014	Screening obstetric ultrasound training for a 5-country cluster randomized controlled trial	Ultrasound Quarterly	Multiple	29	TBD - underway	TBD - underway	Obstetrics & Gynecology NA
Ome-Kaius ³⁴	2017	Effects of Plasmodium falciparum infection on umbilical artery resistance and intrafetal blood flow distribution: a Doppler ultrasound study from Papua New Guinea	Malaria Journal	Papua New Guinea	78	Adjusted odds ratio of doppler measurement associated with increased umbilical artery resistance	2.3 (95% CI 1.0-5.2)	Obstetrics & Gynecology Logiqbook XP, General Electric Medical Systems, UK
Robertson ³⁵	2011	Pilot randomized trial of therapeutic hypothermia with serial cranial ultrasound and 18-22 month follow-up for neonatal encephalopathy in a low resource hospital setting in Uganda: study protocol	Trials	Uganda	40	Risk ratio and absolute difference of mortality in cooled compared to standard care group	5.0 (95% CI) 0.7-37, 0.267 (95% CI 0.029, 0.505)	Pediatrics Zone Ultra Convertible Ultrasound System, 3.0 Release, Zonare Medical Systems Inc. USA

HAND: Handheld echocardiography, RHD: Rheumatic heart disease, CI: Confidence interval

Table 2: Novel prospective ultrasound studies in LMICs*

First Author	Year	Title	Journal	Country	Field	Ultrasound used	Findings	Funding	N	Outcome measure	Outcome
Boamah ³⁶	2014	Gestational Age Assessment in the Ghana Randomized Air Pollution and Health Study (GRAPHS): Ultrasound Capacity Building, Fetal Biometry Protocol Development, and Ongoing Quality Control	JMIR Research Protocols	Ghana	Obstetrics and Gynecology	S180 (Sonosite Inc, Bothell, WA USA)	Use of ultrasound should be considered in field-based trials involving pregnant women to predict GA	NIH	NA	NA	NA
Colquhoun ¹⁶	2013	Pilot study of nurse-led rheumatic heart disease echocardiography screening in Fiji—a novel approach in a resource-poor setting	Cardiology in the Young	Fiji	Cardiology	Model 5 (Mindray, Shenzhen, CN)	Nurses with brief focused training and supervised field experience can follow an algorithm to perform echocardiogram identifying rheumatic heart disease	Cure Kids New Zealand	50	Specificity, sensitivity	100% Nurse A, 83% Nurse B; 67.4% Nurse A, 79% Nurse B
Epstein ³⁷	2018	Pocket-size point-of-care ultrasound in rural Uganda - A unique opportunity "to see", where no imaging facilities are available	Travel Medicine & Infectious Disease	Uganda	Radiology	Vscan GE (General Electric, Milwaukee, WI, USA)	POCUS resulted in change of management	Eldan-Life Sciences	23	Percent of cases in which US image prompted change of clinical management occurred	87.0%
Kimberly ³⁸	2010	Focused maternal ultrasound by midwives in rural Zambia	Ultrasound in Medicine & Biology	Zambia	Obstetrics & Gynecology	S180 (Sonosite Inc, Bothell, WA USA)	Midwives in rural Zambia can be trained to perform basic obstetric ultrasound to improve clinical decision-making	US machines provided by SonoSite	441	Percent of cases in which US image prompted change in clinical decision making	17%

(Contd...)

Table 2: (Continued)

First Author	Year	Title	Journal	Country	Field	Ultrasound used	Findings	Funding	N	Outcome measure	Outcome
Kirkpatrick ³⁹	2018	Focused Cardiac Ultrasound by Nurses in Rural Vietnam	Journal of the American Society of Echocardiography	Vietnam	Cardiology	Model 7 (Mindray, Shenzhen, CN)	Nurses with no prior echocardiographic experience and with limited training can identify patients with significant cardiac abnormalities using FCU with acceptable accuracy	Society of Echocardiography Foundation	8	Specificity, sensitivity, and accuracy of echocardiograms read by nurses	51.5%, 78.1%, 61.9%
Kozuki ⁴⁰	2016	Accuracy of Home-Based Ultrasonographic Diagnosis of Obstetric Risk Factors by Primary-Level Health Care Workers in Rural Nepal	Obstetrics & Gynecology	Nepal	Obstetrics & Gynecology	Nanomaxx (Sonosite Inc, Bothell, WA USA)	With limited training, primary-level health care workers in rural Nepal can accurately diagnose selected third trimester obstetric risk factors using ultrasonography	Children's Prize, National Institutes of Health /Bill and Melinda Gates Foundation / SonoSite	815	Sensitivity, specificity, positive and negative predictive values for 3 auxiliary nurse midwives	90 to 100% for all outcomes of all 3 midwives
Kwan ⁴¹	2013	A simplified echocardiographic strategy for heart failure diagnosis and management within an integrated noncommunicable disease clinic at district hospital level for sub-Saharan Africa	JACC Heart Failure	Rwanda	Cardiology	MicroMaxx (Sonosite Inc, Bothell, WA USA)	Training nurses, supervised by physicians, in simplified protocols and basic echocardiography is one approach to integrated, decentralized care for this vulnerable population	National Scientist Development Award (AHA)	192	Observed mortality with long-term nurse follow-up (comparable to non-nurse follow up data)	0.09

(Contd...)

Table 2: (Continued)

First Author	Year	Title	Journal	Country	Field	Ultrasound used	Findings	Funding	N	Outcome measure	Outcome
Leopold ⁴²	2018	Point-of-care lung ultrasound for the detection of pulmonary manifestations of malaria and sepsis: An observational study	PLoS ONE	Bangladesh	Pulmonology	GE Healthcare Vivid-I Portable (General Electric, Milwaukee, WI, USA)	LUS was highly feasible and allowed accurate identification of patients at risk of death in a resource limited setting	Wellcome Trust	102	Percentage of patients who died with lung US abnormalities	86%
Lu ⁴³	2015	Simplified rheumatic heart disease screening criteria for handheld echocardiography	Journal of the American Society of Echocardiography	Uganda	Cardiology	GE Vivid q or i or Philips CX-50 (General Electric, Milwaukee, WI, USA)	In resource-limited settings, HAND with simplified criteria can detect rheumatic heart disease with good sensitivity and specificity and decrease the need for standard echocardiography	NIH National Center for Advancing Translational Sciences	1439	Mitral regurgitation detection sensitivity and specificity	73.3% 82.4%
Madimenos ⁴⁴	2011	Normative calcaneal quantitative ultrasound data for the indigenous Shuar and non-Shuar Colonos of the Ecuadorian Amazon	Archives of Osteoporosis	Ecuador	Orthopedics	Sahara bone sonometer (Hologic, Inc., Waltham, MA, USA)	In both populations and sexes, all calcaneal QUS values were progressively decreased with advancing age. These normative data for calcaneal QUS parameters will be useful for predicting fracture risk and determining diagnostic criteria of osteoporosis in these populations	Wenner-Gren Foundation; NSF Evonuk Foundation; Leakey Foundation; Ryoichi Sasakawa Young Leaders Fellowship; NIH	488	Difference in calcaneal QUS values between Shuar and Colonos	P < 0,001

(Contd...)

Table 2: (Continued)

First Author	Year	Title	Journal	Country	Field	Ultrasound used	Findings	Funding	N	Outcome measure	Outcome
Mand ⁴⁵	2011	The role of ultrasonography in the differentiation of the various types of filaricercle due to bancroftian filariasis.	Acta Tropica	Ghana	Urology	S180 Plus (SonoSite Inc, Bothell, WA USA)	In an unexpected high number of men, fluid accumulation around the testis was detected by those in clinical US, of which more than one third presented with subclinical stages.	Bill and Melinda Gates Foundation	1453	Patients without hydrocele and subclinical disease had thinner scrota skin than those in clinical stages with lymphscrotum	P < 0.001
Michels ⁴⁶	2013	The predictive diagnostic value of serial daily bedside ultrasonography for	PLoS Neglected Tropical Diseases	Indonesia	Infectious Disease	Signos personal ultrasound	Serial ultrasonography, in contrast to existing markers such as hematocrit, may better identify patients at risk for development of severe dengue	Rdaboud University Nijmegen Medical Center	77	Positive predictive value and negative predictive value for severe dengue of subclinical plasma leakage seen on US	35%, 90%
Michels ⁴⁶	2013	The predictive diagnostic value of serial daily bedside ultrasonography for severe dengue in Indonesian adults.	PLoS Neglected Tropical Diseases	Indonesia	Infectious Disease	Signos personal ultrasound	Serial ultrasonography, in contrast to existing markers such as hematocrit, may better identify patients at risk for development of severe dengue	Rdaboud University Nijmegen Medical Center	77	Positive predictive value and negative predictive value for severe dengue of subclinical plasma leakage seen on US	35%, 90%
Mirabel ⁴⁷	2015	Screening for rheumatic heart disease: evaluation of a focused cardiac ultrasound approach.	Circulation. Cardiovascular Imaging	New Caledonia	Cardiology	V-scan (General Electric, Milwaukee, WI, USA)	FCU by nonexperts using pocket devices seems feasible and yields acceptable sensitivity and specificity for rheumatic heart disease detection when compared with the state-of-the-art approach	French Federation of Cardiology	1217	Sensitivity and specificity of FCU to detect rheumatic heart disease by two nurses	83.7% Nurse A, 77.6% Nurse B; 90.9% Nurse A, 92.0% Nurse B

(Contd...)

Table 2: (Continued)

First Author	Year	Title	Journal	Country	Field	Ultrasound used	Findings	Funding	N	Outcome measure	Outcome
Murphy ⁴⁸	2011	Ultrasound findings in Plasmodium falciparum malaria: a pilot study	Pediatric Critical Care Medicine	Uganda	Pediatrics	Micromaxx (Sonosite Inc, Bothell, WA USA)	A targeted ultrasound examination focusing on optic nerve sheath diameter, color transcranial Doppler, cardiac ultrasound, and spleen size may prove useful for patient classification, risk stratification, research studies, and treatment monitoring in pediatric malaria	Department of Pediatrics, Massachusetts General Hospital for Children.	33	Increased optic nerve sheath diameter in patients with malaria, and in patients with cerebral malaria	33%, 100%
Ploutz ⁴⁹	2016	Handheld echocardiographic screening for rheumatic heart disease by non-experts	Heart	Uganda	Cardiology	GEVscan V.i.2 (GE Medical Systems, Milwaukee, WI, USA)	Non-expert-led HAND screening programmes offer a potential solution to financial and workforce barriers that limit widespread rheumatic heart disease screening	NIH and National Center for Advancing Translational Sciences; General Electric Foundation	1002	Simplified approaches sensitivity and specificity to diagnose rheumatic heart disease	74.4% (58.8% to 86.5%) / 78.8% (76.0% to 81.4%)
Reynolds ⁵⁰	2016	Bedside ultrasound training at Muhimbili National Hospital in Dar es Salaam, Tanzania and Hospital San Carlos in Chiapas, Mexico	African Journal Of Emergency Medicine	Tanzania	Internal Medicine	DP3300 (Mindray, Shenzhen, CN)	Introducing bedside ultrasound training in two distinct resource-limited settings was feasible and well-received	Abbott Fund, UCSF Global Health Sciences; Sonosite	22	Pass rate of final exam at both sites	100%

⁴⁸All novel ultrasound studies with prospective design, funding source and model of ultrasound used. GA: Gestational age, NIH: National Institutes of Health, NA: Not applicable, POCUS: Pocket-sized point-of-care ultrasound, FCU: Focused cardiac ultrasound, LUS: Lung ultrasound, HAND: Handheld echocardiography, QUS: Quantitative ultrasound

that nearly 70% of studies involved ultrasound usage originating from Southeast Asia and sub-Saharan Africa. In terms of novel ultrasound research conducted in LMICs, the region with the most studies was Western and sub-Saharan Africa (46.7%), driven by research conducted in Nigeria, Uganda, and Tanzania. 72% of studies involved global collaboration, meaning an author from an LMIC was present in the final publication. This lack of representation of authors from LMICs indicates that global collaboration could and should be increased, with the goal of 100% of research efforts and the subsequent academic publications involving collaboration with LMIC partners in the country where the research was conducted. This represents a potential lack of representation seen in other areas of publication.

Focus of Studies

The majority of ultrasound studies focused on cardiology, which described usage of portable echocardiograms, and obstetrics where the use of ultrasound in prenatal care is standardized. Pediatric care, gastroenterology, and internal medicine were specialties that conducted substantial research with ultrasound in the LMICs. Looking at novel applications of ultrasound, we found the increasing application of US as a screening tool was utilized, with novel applications including screening for Crimean-Congo hemorrhagic fever in Turkey,⁶ human cystic echinococcosis in Morocco,⁷ and dengue fever severity in India.⁸ Other noteworthy applications of novel ultrasound research included the deployment of a wind-up powered fetal heart monitor in Uganda conducted by Byaruhanga et al⁹ and the development of a machine learning model to classify chronic liver disease severity based on liver ultrasound in India by Bharti et al.¹⁰

Types of Studies

Many studies on the use of ultrasound in LMICs were qualitative studies understanding the perceptions of ultrasound use, most commonly examining community perceptions of routine ultrasound imaging during pregnancy. Of note, perceptions about routine prenatal ultrasound care among physicians, midwives, and patients were studied. For example,

the use of ultrasound in standard prenatal care was measured in several countries, as it represented a new phenomenon and was found to be essential to improving maternal outcomes. Key studies conducted in Tanzania, Uganda, Nigeria, Ghana evaluated the changing perception of obstetric ultrasound use for prenatal care.¹¹⁻¹⁴ We found that 'novel ultrasound research' was published more often in international journals than 'applications of ultrasound' studies, which were commonly published in regional journals, i.e. PLoS ONE versus the Indian Heart Journal.

Educational Programs

We found that the rate of educational studies remained relatively consistent over the period studied. However, many of the educational studies focused on task-shifting from skilled providers to training for lay providers including midwives, medical students, community health workers, or other lay people. This includes the emerging role of teleconsultation services and tele-imaging in ultrasound around the world. For example, Bansal et al conducted the VISION-in-Tele-Echo study which evaluated the benefit of a teleremote training program in echocardiography in India, and Colquhoun et al conducted a pilot study of nurse-led rheumatic heart disease echocardiography screening in Fiji.^{15,16} Furthermore, some studies combined educational training programs alongside a measurable impact on increased screening and diagnosis. The study conducted by Chamadol et al outlined the teleconsultation program launched in Thailand for the diagnosis of cholangiocarcinoma, while simultaneously capturing the additional patients screened and health centers impacted by the program.¹⁷ Finally, the availability of ultrasound gel was identified as a potential barrier to use due to cost and lack of availability of commercially produced ultrasound gel.¹⁸ Several studies outlined low cost recipes for generic ultrasound gel, including the use of shampoo, Guar Gum, corn starch, lotion, and Betadine.¹⁸⁻²⁰

Overall Trends

Our study identified the overall trend of increasing studies in ultrasound application in LMICs over

the past decade. There has been increased use of ultrasound with new applications of technology simultaneously focused on the increased application in rural health care centers. Furthermore, research in ultrasound studies indicates a trend of increased training programs, using teleremote technologies to expand task shifting to lay providers, and ingenuity in using this low-cost technology in new ways adapted for low-resource settings. The findings outlined in the literature indicated the increased scope of ultrasound and its use in LMICs, where such a low cost, portable, diagnostic imaging modality is an extremely valuable tool. Furthermore, the study has identified the potential for hand-held technology to make this imaging modality widely available at a potentially low cost. Care providers should keep in mind barriers to use, including patient and provider perceptions, level of skill, power availability, and the lack of technical repair when designing ultrasound related programs on a global basis.

Limitations

There were several limitations in this study. LMIC economies as defined by the World Bank differ from year to year, therefore, the countries identified in 2018 may not include relevant countries from previous years, or include countries recently added to low or lower-middle economies. The Cochrane risk of bias assessment tool found that nearly one-half of the novel ultrasound research in the form of randomized controlled trials had a high or medium risk of bias, therefore conclusions derived from those specific studies should be considered carefully. Our definition of ‘novel ultrasound research’ involved some subjectivity and may represent biased inclusion of studies in this category. We attempted to minimize this bias by double-screening for inclusion. Finally, this study consists of a 9-year time frame, so may not capture longer-term trends.

Recommendation for Further Studies

We recommend further study promoting global collaboration, especially with inclusion or leadership by authors affiliated with institutions within LMICs, potentially still in collaboration

with or funded by external institutional partners. Furthermore, the majority of studies were conducted within four countries (India, Egypt, Pakistan and Nigeria), and were performed at tertiary care centers. Further studies in lower-income economies and within district hospitals or community healthcare centers would broaden our scope of knowledge of ultrasound applications and adaptability to low-resource and rural settings.

5. Conclusion and Global Health Implications

In conclusion, this literature review focused on ultrasound trends and usage in LMICs. With the decreasing cost of ultrasound equipment and increasing availability of handheld ultrasound devices, it is important to continue assessment of the adoption and effective novel application of ultrasound technology in LMICs. Furthermore, there is a pressing need to address the potential capabilities and delineate limitations of ultrasound within resource limited settings. We found evidence of the role of educational training programs increasing screening and diagnostic clinical decision making. We also found the increasing adoption of ultrasound technology globally.

Compliance with Ethical Standards

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Key Messages

- Ultrasound related research and associated applications of this technology in LMICs has increased over the past decade.
- The role of educational training programs increasing screening and diagnostic clinical decision making was identified.
- There is a need for greater global collaboration in addition to higher quality ultrasound related research in LMICs.

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