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Barriers To Accessing Assisted Reproductive Technology in Low- And Middle- Income Countries: A Systematic Review

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ABSTRACT : Background: The advent of assisted reproductive technology (ART) has significantly aided addressing fertility issues. However, equitable access to this intervention in low- and middle- income countries (LMICs) has been shown to be a major challenge due to several barriers. Socio-economic determinants including, but not limited to financing, cultural connotations and literacy have been shown to affect health service utilisation in low resource countries.
Aim: The present study aimed to systematically review relevant literature on various barriers to accessing ART services in LMICs and interventions in overcoming them.
Method: A comprehensive search was conducted in 5 electronic databases **(**Web of Science, PubMed, Science Direct, CINAHL Ultimate**,** MEDLINE), with MeSH terms using the SPIDER framework. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (2020) guideline was employed for this review. 10 articles were included in the systematic review using the eligibility criteria and critical appraisal based on the Critical Appraisal Skill Programme (CASP) and Joanna Briggs Institute (JBI). Data was synthesised using thematic analysis.
Results: The results demonstrated that cost of infertility treatment, situation of fertility centers as well as residential area of patients, poor knowledge, wrong perception, beliefs and social influences are barriers to accessing and utilising ART. The distribution of these wider determinants of health were shown to result in inequities and inequalities in accessing assisted reproductive technology. Some of these barriers were mutual with high income countries but the absence of funding and policies have made the consequences of infertility more impactful in low- and middle- income countries.
Conclusion: The impact of these barriers will continually be felt in low- and middle- income countries unless there are significant strides in supporting sustainable access to ART. The presence of policies to regulate ART, subsidising of fertility treatments, proper sensitisation of the public with the inclusion of leaders of the society are some of the actions which may enhance access to ART.
KEYWORDS : *Assisted reproductive technology, low- and middle- income countries, health inequalities, barriers to accessing infertility treatment.*

I. INTRODUCTION

Infertility affects 48.5 million couples globally with a prevalence of about 3.5–16.7% in low- and middle-income countries (LMICs), of which 30–40% of this is recorded in Sub-Saharan Africa [1, 2]. To combat infertility, assisted reproductive technology has been utilised globally in treating various forms of infertility [1, 2]. However, its services are not accessible to most of the infertile couples in LMICs due to health inequalities and the unequal distribution of ART clinics [1,3,4,5,6,7]. This presents challenges in addressing fertility issues in LMICs, thus calling for appropriate sustainable interventions. Infertility and its treatment are not prioritised in many LMICs due to competing health needs for limited resources [3]. Although infertility is not a direct cause of death, its consequences ranging from intimate partner violence, social isolation, mental health issues, shame and stigma evidently demonstrate that infertility is a reproductive, social and public health issue, particularly in some cultures where childbirth only secures a woman's marriage and a place in her family [8,9,10,11]. Relevant literature has stressed the consequences of infertility thus establishing the need for systematically assessing the challenges associated with accessing ART in LMICs.

II.MATERIALS AND METHODS

2.1. Study Design

This systematic review included qualitative and quantitative primary research studies which explored the barriers of accessing reproductive health technology

2.2. Search Strategy

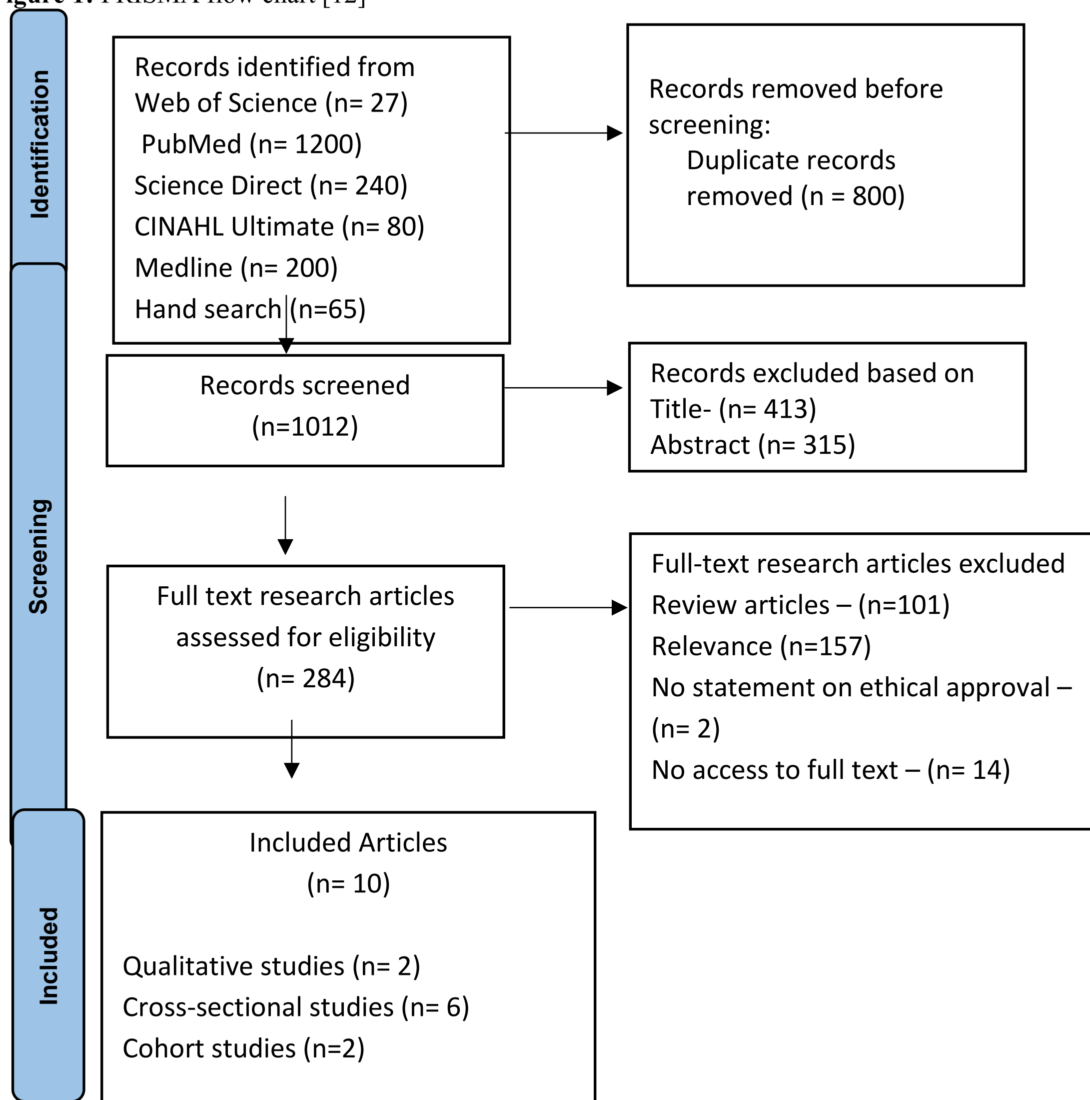
To justify the need for this systematic review, literature review was initially conducted on PubMed, Google Scholar and CINAHL ultimate databases in line with the Centre for Reviews and Dissemination 2009 guidelines. Cochrane Database of Systematic Reviews was searched for ongoing or existing systematic review being carried out. Different systematic reviews were found regarding various barriers to accessing ART in different countries but there was no systematic review addressing the barriers to accessing ART in LMICs as a region.

In line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for systematic reviews, a comprehensive search of databases was conducted to find relevant publications. The literature search was across countries categorized as LMIC to minimize bias. MeSH terms like "IVF" "Assisted Reproduction" "Assisted Reproductive Technology" Infertility" and Boolean Operators AND & OR were used to narrow the search. The search was further narrowed with filtering using the eligibility criteria. Hand search was done to identify more relevant studies. The databases search resulted from 27, 1,200, 240, 80, 200 and 65 from Web of Science, PubMed, Science Direct, CINAHL Ultimate, Medline and hand search respectively.

2.3 Study selection

After database search, 1,812 articles were found. 800 articles were removed for duplication to using Endnote and were screened manually, 413 during screening of title because they are not original articles or were conducted in other countries not considered LMIC,315 were removed during abstract screening, 258 excluded during full-text evaluation, 14 were excluded for no access and 2 for no ethical approval, leaving 10 papers for final inclusion in this systematic review as shown in Fig 1.

Figure 1: PRISMA flow chart [12]



2.4 Ethical Consideration

The University of Sunderland in London Research Ethics group determined that there was no need for ethical consent. This is because systematic reviews only require retrieving and synthesizing secondary data from articles published previously.

2.5 Eligibility Criteria

Only original articles conducted in countries categorized as Low- and Middle- Income according to World Bank Classification were included [13]. However, the study population included adults infertile couples from age 18 with no age limit as ART has been recorded to be performed with advanced maternal age in some LMICs [14]

(Table 2).

Table 2: Eligibility Criteria

	Inclusion Criteria	Exclusion Criteria
Sample	Infertile couples in LMICs	Infertile couples in High income countries
Phenomenon of Interest	Barriers to accessing ART and Intervention to overcoming them in LMICs	Barriers to accessing ART in High- Income- Countries
Design	Primary qualitative research, cross-sectional studies, cohort studies, and mixed method research.	Experimental studies and Reviews
Evaluation	Identifying the barriers to accessing ART in LMICs and the existing interventions.	Information and evidence not regarding the subject topic.
Research Type	- Only articles published in English language. - Peer-reviewed articles. - Research papers published between 2013 and 2023 - Qualitative and quantitative studies	Articles published in other languages Grey literature, case studies Reviews, editorials, government reports and Research papers published before 2013.

2.6 Data extraction and quality assessment

Data was extracted per article into a Microsoft Excel spreadsheet with the following study characteristics; first author, year of publication, aims and objectives, study design, sampling technique, country, participants, outcomes, outcomes and recommendations reported, and the themes identified from each study.

Quality assessment to examine the studies' methodological weaknesses, strengths, trustworthiness, validity of the research, of the results, and presence of biases skills program was applied to the 10 studies using Critical Appraisal Skills Programme (CASP) and Joanna Briggs Institute (JBI) critical appraisal tools [15, 16] **(Table 3).**

2.7 Data Analysis

It was decided a systematic review was the best approach because of the heterogeneity of the included articles. Therefore, thematic analysis using the Bruan and Clarke [17] method was used for data synthesis from the included studies.

Table 3.0: Quality assessment of included qualitative studies using CASP tool [15].

	SECTION A: Are the results valid?						**SECTION B: What are the results?**			**SECTION C: Will the results help locally?**
Reference	Was there a clear statement of research aims	Is qualitative methodology appropriate?	Was the research design appropriate to address the aims of the research?	Was the recruitment strategy appropriate to the aims of the research?	Was the data collected in a way that addressed the research issue?	The relationship between researcher and participants been adequately considered?	Have ethical issues been taken into consideration?	Was the data analysis sufficiently rigorous?	Is there a clear statement of findings?	How valuable is the research?
Ezeome et al (2023) [18].	-	+	+	+	+	+	+	+	+	+
Okantey, et al (2021) [19]	+	+	+	+	+	+	+	+	+	+

Table 3.1: Quality assessment of included cohort studies using CASP tool [15]

	SECTION A: Are the results valid?								**SECTION B: What are the results?**			**SECTION C: Will results help locally?**		
Reference	Did the study address a clearly focused issue?	Was the cohort recruited in an acceptable way?	Was the exposure accurately measured to minimise bias?	Was the outcome accurately measured to minimise bias?	Have the authors identified all important confounding factors?	Have they taken account of the confounding factors in the design and/or analysis?	Was the follow up of subjects complete enough?	Was the follow up of subjects long enough?	What are the results of this study?	How precise are the results?	Do you believe the results?	Can the results be applied to the local population?	Do the results of this study fit with other available evidence?	What are the implications of this study for practice?
da Silva et al (2019) [20]	+	+	+	+	+	+	+	+	+	+	+	-	+	+
Dyer et al (2013) [21]	+	+	+	-	+	+	+	+	+	+	+	-	+	+

Table 3.2: Quality Assessment of included cross-sectional studies using JBI critical appraisal tool [16].

Reference	Were the criteria for inclusion in the sample clearly defined?	Were the study subjects and the setting described in detail?	Was the exposure measured in a valid and reliable way?	Were objective, standard criteria used for measurement of the condition?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the outcomes measured in a valid and reliable way?	Was appropriate statistical analysis used?
Chikeme et al (2021) [22].	+	+	+	+	-	-	+	+
Okafor et al (2017) [23].	+	+	+	+	-	+	+	+
Olorunfemi et al (2021) [24].	+	+	+	+	-	-	+	+
Harzif et al., (2019) [25].	+	+	+	+	+	-	+	+
Oche et al (2018) [26].	+	+	+	+	-	+	+	+
Adenike et al (2014) [27].	+	+	+	+	-	-	+	+

(+) = item adequately addressed, (-) = item not adequately addressed, NS= not stated or not clear, NA= not applicable.

2.7 Outcome of Critical appraisal

All the 10 studies that were critically appraised were considered of good quality and were included in this review. However, some studies [18,19,29] had a lesser sample size compared to the rest [21,22,23,24, 25,26,27]. These studies were also included because they address the scope of the problem. Cohort and qualitative studies depict better assessment scores than cross-sectional scores. The variation in the scores may be because of the study design, as most cross-sectional studies failed to highlight confounders and possible ways to control them.

III.RESULTS

3.1 Characteristics of the Included Studies

Overall, this systematic review describes a population of 2,071 participants from 5 countries that are classified as LMICs. 10 articles were included after screening and quality assessment. The study designs were qualitative (n=2), Cohort (n=2) and Cross-sectional (n=6) **(Fig 1).** Out of the 10 included studies, 6 were conducted in Nigeria, 1 in Ghana, 1 in South Africa, 1 in Brazil, and 1 in Indonesia. The publication dates ranged between 2013 and 2023. 1 article was published in 2013, 1 in 2014, 1 in 2017, 1 in 2018, 2 in 2019, 2 in 2021, 1 in 2022 and 1 in 2023.

The sample size varied between 8 and 600.

- **Table 5.** Themes generated from included studies.

	THEMES	SUBTHEMES
1	Financial burden	Expensive cost of ART.
		Financial challenges.
2	Information on ART	Healthcare providers, media, family and friends were sources.
		Lack of information on how to access ART centers.
3	Knoledge, AWARENESS, BELIEFS, AND PERCEPTION OF ART SERVICES.	Fetuses from ART are deformed.
		ART causes congenital anomalies.
		Religious belief, belief in the supernatural.
		Unavailability of clinics.
4	SITUATION OF ART CLINICS	More clinics are in urban areas.
		People travel farther distances to access ART services.
5	SOCIAL CHALLENGES	Cultural bias, stigmatisation

3.2 Financial burden is a barrier to accessing ART services.

ART is unaffordable for an average Nigerian woman and this lack of fund from participants prevented early access to ART services which is similar to the findings in Ghana [18,22,19]. In South Africa, Nigeria, and Brazil, income was found to strongly correlate to ART use and confirming the outrageous amount participants pay for ART out of pocket thereby causing the poorer household to suffer more and have little or no access ART services [20,21,24,27]. While some participants complained of having no more money after using ART services, some others would love to have another child through ART but the cost and financial constraints act as a barrier. This establishes some inequality in access to healthcare where women of higher socioeconomic status, better employment and higher education accessed ART services.

3.3 Type and source of information on ART services impacts knowledge and perception of art services.

In relation to the study objectives, sources of information are known to impact medical knowledge [29]. Participants in Nigeria have identified the sources of information as social media, internet, family and friends which are considered as wrong sources [26,18] and ART practitioners; the ideal source [22,27]. Ezeome et al., (2023) opined that there was lack of information on how to access ART services, causing vulnerable patients to be exploited by fake and inexperienced practitioners with a risk of death to complications of the procedures. The presence and fear of complications of the procedures act as a barrier to the utilization of infertility treatments. Aside from these, there was inadequate information on the risks and benefits of the procedures [18,19].

3.4 Knowledge, awareness, beliefs, and perception of ART services are barriers to accessing art services.

Some studies in Nigeria established that there is average knowledge, awareness, positive perception on ART services [22,26,27], while some disagree both in Nigeria and Indonesia where there was erroneous knowledge among both rural and urban participants [23,25,27]. Participants also perceive children born through ART will have abnormalities, are unnatural and may not be socially accepted as well as a high level of disbelief and suspicion in the efficacy of ART services [27]. Olorunfemi et al (2021) reports that the utilization of ART services is dependent on the perception of spouses about the procedures [18,24]. Religious and spiritual beliefs also have been identified as possible barriers. Participants would rather turn to traditional means or "black magic" rather than medical means [18,25,26,23,24]. These beliefs range from perceiving infertility as a punishment to destiny from a supreme being [19]. Although Ezeome et al., (2023) reported that half of the participants in Nigeria who were Christians (Catholic) utilized the services despite their doctrine forbidding the utilization of ART services [18].

3.5 Situation or location of ART clinics influences its access.

Most ART services are in larger regional or metropolitan areas which is a geographical barrier [29]. Similarly, fertility clinics are reported to be in urban areas with bad roads leading to them. This has attributed to failed cycles in Nigeria and Brazil [20,18, 23]. One study conducted in Ghana revealed the cost associated with patients seeking infertility who live far away from ART centers [30]. This also means that couples seeking treatment in rural areas will incur additional cost to access it which is not peculiar to LMICs as studies in Australia revealed [31,32].

3.6 Subjective norm within society posits a barrier to accessing ART services.

ART or IVF is tagged unnatural therefore its utilization comes with shame and stigmatization [23,18,20,27]. ART in Ghana contradicts the social ethics of childbearing and poses challenges to its acceptance and utilization. Participants are concerned about the feelings, stigmatization and attitudes of people in society, their spouses or partners and extended family, towards them and their children due to their use of ART services [19]. Cultural bias like a woman must conceive and carry her child by herself, rather than using a surrogate exists [22,23,24]

IV. DISCUSSION

The findings from this study and many others report that socioeconomic status, education and employment as well as residential area contribute to reduced access to ART services in LMICs. One of the most reported barriers in this systematic review is Finance. ART is costly, unaffordable and inaccessible to those who need it regardless of the countries being categorized as middle- or lower-income countries. This has however been linked with the impacts of other wider social determinants of health which entails reasonable inequalities in LMICs, and the out-of-pocket healthcare system practiced in LMICs. [33,3,34,35,36] A study reported in Thailand and Bangladesh that ART costs between US$2,900 per cycle in government hospitals and US$5,800 in private clinics with people's average per capita income is estimated to be US$240 monthly, which is corroborated by a recent systematic review on the financial implication of infertility treatment in LMICs [37,38,39].

Evidence show that female educational level contributes to the use of ART even though the exact mechanisms in this relationship remain complex and multifactorial [40,41,42]. One possible explanation is educated women are very knowledgeable, aware of ART services and opt for it as a solution when faced with infertility, compared to women with lower levels of education as they might face barriers to accessing infertility treatments [27]. This together income level may contribute to the relationship between education, female infertility and access to healthcare. Women who have higher levels of education may have higher incomes and better access to healthcare which extends to being able to afford ART services [43]. This further points at the need of comprehensive reproductive health education for all women regardless of the level of education and income level in order to overcome this existing inequality. Conversely, higher education does not totally equate to accessing ART services as women pursuing higher education levels may delay childbearing in order to focus on their careers or educational goals thereby causing them not to access or utilize the services where correct and adequate information reside especially on the impact of advanced maternal age on fertility and birth outcomes [44,43,45,42].

The cost of ART is already expensive but having to travel miles to get treatments incurs additional cost when travel and accommodation expenses are summed up [47]. It is reported that three-quarters of the infertility clinics in Thailand are situated in urban areas, thereby favoring people settled in Urban area and causing disparity in access to ART treatment [37,25]. This inequality is not peculiar to LMICs, as higher income countries like the United States of America (USA), Australia and Japan with funding for infertility treatment have reported similar inequality which compounds the problem, as patients are far away from their comfort area as well as support system such as family members [32,48,49,50,51]. Geographical location is not just a barrier but also a determinant to the type of treatment offered as patients in urban areas are more likely to get effective infertility treatments [52,53]. Again, because of this inequality, patients in rural areas may get delayed diagnosis of their infertility. Therefore, safe and effective treatment is required regardless of the patient's settlement.

The level of awareness and knowledge of ART also impacts how well it will be accessed [56,46]. There is low to average level of awareness and knowledge of ART influenced by various factors that prevent people from accessing ART. These include myths that children born through ART have abnormalities or are unnatural, religious beliefs, experiences of others who have utilized ART, presence of ART centers and its distribution among rural and urban areas. For example, the Gambia, even with reduced number of IVF centers report reasonable level of knowledge among health practitioners and medical students which is expected, the survey further notes that awareness of the public is low [54]. Similar findings were reported in northern Nigeria, Pakistan, Egypt, South Africa, Rwanda, Angola, Zambia, and Mozambique [55,36,57,58,59,60,61]. These significant and valid barriers can be overcome by sensitizing the public to reduce stigmatization, wrong beliefs and practices [62,63,64].

In as much as this inequality is mutual to most countries regardless of income level, funding from the government of higher income countries makes the difference. The lack of support and funding of ART services by LMICs government has made ART services out-of-pocket payment, which many households cannot afford. This means ART services can only be accessed by the rich [65,50,21,66]. Although, there have been no reports of state-funded ART treatments in Sub-Saharan Africa, affordable ART treatments have been introduced in some countries like Uganda, South Africa, and Nigeria [35,67,68]. Practices of ART in Sub-Saharan Africa are quite similar to high-income countries although absence of guidelines, legislation and regulatory body like where the Human Fertilization and Embryology Authority (HFEA) in the United Kingdom exist have made ART clinic in this region base their practices on European/American guideline, neglecting the fact these developing countries are heterogeneous with diverse culture, moral values, religions, and beliefs. Although the Association for Fertility and Reproductive Health of Nigeria (AFRH) is active as a regulatory body to provides ethical guidelines for ART, there still no representation in legislation [69]. Bamgbopa et al (2018) however opines that the representation in legislation is the duty of both AFRH, the society of Obstetrics and Gynecology of Nigeria (SOGON), and the Nigerian Medical Association (NMA) [70].

V.LIMITATIONS

- Causal relationship could not be established as most of the included studies are cross-sectional study design.
- Possible confounding risk, as most included studies did not consider the likely interaction of confounding factors in the outcomes.
- Most participants are female, thereby showing selection bias.
- The number of participants in various studies are small and therefore do not give a robust picture of the reality of the problem of poor access to ART and inequalities in the use of ART. It undermines the internal and external validity of this study.
- This review excluded studies written in other languages which may include other barriers

The presence of such statutory body in LMICs will address many barriers recorded in LMICs. It will ensure health inequalities are identified and addressed and health surveillance**.** It is comforting to know that the Brazilian and Mexican government in 2012 provided measures like financial support and laws to develop standards of

practice for assisted reproduction services [71,72,73]. This act will address the lack of trust people have in ART procedure and its success as there is cohesiveness of all actors in ensuring that quality care is delivered to people. Together with results from this study, the government has consistently been called upon to intervene by creating policies and commissioning to improve access to ART for infertile couples and overcome all these barriers.

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