Review Article

Fetal imaging and diagnosis services in developing countries – A call to action

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ABSTRACT

Fetal congenital anomalies are among the leading causes of perinatal death or survival with disability worldwide. Their accurate antenatal detection employing a range of fetal imaging techniques enables parental choices to be made and for postnatal care of affected babies to be planned. While such prenatal care is well developed in developed countries of the world, it remains poor in many low- and middle-income countries (LMICs). This review article examines the scope of the problem and proffers strategies for service organization and fetal imaging that will improve care in LMIC settings.

Key words: Congenital abnormalities; fetus; imaging; pregnancy; ultrasound.

Introduction

Congenital anomalies are among the leading causes of perinatal morbidity and mortality worldwide and represent a significant challenge to public health globally.[1] According to the World Health Organization (WHO) and other sources, major congenital anomalies affect 2%–3% of infants worldwide with a greater proportion occurring in developing countries and communities where consanguineous marriage is rife.[1-3] It is also estimated that 20%–30% of global neonatal deaths are due to congenital anomalies, with 95% of all such deaths occurring in the low- and middle-income countries (LMICs).[1]

The incidence of congenital anomalies varies from country to country and is reported to be as low as 1.1% in Japan and as high as 4.3% in Taiwan. Most prevalence rates reported from other countries fall within this range: 2%–3% in the United Kingdom, 1.5% in South Africa, 3% in the United States, and 3.65% in India.[1] The birth prevalence in the developing world is underestimated due to deficiencies in diagnostic capabilities and lack of reliability of medical records and health statistics.[4,5] Given the paucity of data from developing countries, reliance for estimating the quantum of the problem is placed on hospital-based studies. In some of such studies in Nigeria, the prevalence of congenital anomalies was reported as ranging between 0.5% and 9.9%.[6-10]

Although the major risk factors for congenital anomalies are advanced maternal age, chromosomal abnormalities, mutant genes, and teratogenic agents, no specific risk factor is identifiable in 80%–90% of cases. Because of this, early prenatal diagnosis by fetal imaging is the principal diagnostic approach for detecting anomalies, thus optimizing care, reducing perinatal morbidity and mortality, and enhancing parental choice of either continuing with a pregnancy with major anomalies or terminating it.[11-13]

In this review, we are highlighting the gaps in the delivery of fetal diagnostic services in developing countries, based on

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Access this article online	
Website: www.tjogonline.com	Quick Response Code
DOI: 10.4103/TJOG.TJOG_59_18	

How to cite this article: Akinmoladun JA, Anumba DO. Fetal imaging and diagnosis services in developing countries – A call to action. Trop J Obstet Gynaecol 2019;36:1-7.

the modalities for fetal imaging employed for detection and management of congenital anomalies. We suggest potential strategies for improving fetal screening and diagnosis by a more coordinated approach to the planning, organization, and delivery of these services in resource-limited economies.

Fetal Imaging in Prenatal Screening and Diagnosis

In the past four decades, the development of screening for fetal anomalies has profoundly affected perinatal care in most developed countries.[14-16] This has been due mainly to advances in prenatal imaging (such as ultrasonography with Doppler and ultrafast magnetic resonance imaging [MRI]) and biochemical techniques, as well as the more widespread availability of specialist training in fetal anomaly imaging.

Ultrasonography: 2-Dimensional ultrasound (US) has been the principal method of imaging fetal abnormalities in the developed world.[16-18] Recently, the introduction of three- and four-dimensional US has been reported to enhance the assessment of specific fetal anomalies, although these modalities have not been consistently shown to improve overall detection rates of fetal anomalies[19-21] especially when particular organs such as the brain,[22] heart,[23] face, and palate are being evaluated.[24,25] Early pregnancy US was initially introduced for the purpose of determining fetal viability, measuring crown-rump length to achieve accurate pregnancy dating, determining pregnancy location, and determining fetal number and chorionicity, in multiple pregnancies.[26-29] Mid-trimester ultrasonography between 18 and 21 weeks has traditionally enabled imaging to screen and detect fetal structural anomalies. With the advent of transabdominal and transvaginal high-frequency transducers, sonologists are now able to image the fetus in greater detail at all gestational ages.[26-28] Some anomalies will nearly always be detectable in the first trimester, e.g., anencephaly, holoprosencephaly, facial cleft, and conjoined twins.[30,31] However, many (e.g., fetal heart anomalies) remain too subtle to be detected that early, requiring second trimester scanning.[32,33] The introduction of Doppler technology for fetal imaging has also improved the detection of fetal anomalies especially in the area of fetal echocardiography.[31,33,34] Although all of these techniques are routinely available in most maternal healthcare facilities in developed countries, they remain largely unavailable, inaccessible, or unaffordable in resource-poor countries with rudimentary fetal care services.[35-37]

Magnetic resonance imaging: Ultrasonography has limitations when employed to detect fetal anomaly. Image resolution may be limited due to fetal position and movement, reduced amniotic fluid volumes, maternal obesity, and the state of filling of the maternal bladder. In such situations, repeated examinations may be required. MRI has emerged as a complimentary imaging modality for assessing the fetus and is now widely available in many developed countries, when a sonographic abnormality is detected or suspected and further diagnostic information is considered useful in pregnancy management. It has been reported to have little or no adverse impact on the mother and fetus, although its safety in first trimester has not been fully evaluated.[17,38] Many studies have reported that fetal MRI allows more detailed observation than prenatal US and therefore provides additional information to confirm or change a diagnosis and possibly alter clinical care.[17,21,39-41] There is emerging evidence of this added benefit when assessing the fetal central nervous system (CNS), congenital diaphragmatic hernias, and abnormalities of the genitourinary system. It is, however, not recommended as a primary imaging modality but as an adjunct to US for prenatal diagnosis.[19,41] This is on account of its cost, availability, and ease of use.[17,19] Considerable expertise is required for its interpretation, a fact that militating against its adoption for fetal imaging in resource-poor countries, where ultrasonography is virtually the sole imaging modality available for prenatal diagnosis.[42,43]

Management Options Following Prenatal Diagnosis

Accurate diagnosis of fetal anomalies enables couples to make informed choices regarding the care provided to them. Earlier detection of fetal structural abnormalities allows for earlier decision-making regarding whether to terminate the severely affected fetus or to refer the mother for care and delivery at a tertiary center staffed by the appropriate specialists.[44,45]

Prompt referral of cases of congenital anomalies at the time of prenatal diagnosis has greatly influenced optimization of care, thus, improving perinatal mortality and morbidity in the developed countries.[44,46]

Although termination of pregnancy at a wide spectrum of gestations is possible in most developed countries, restrictive abortion laws, and lack of expertise and facilities preclude this as an option in many developing countries of the world.[47,48] In the latter settings, fetal autopsy to clarify the fetal diagnosis and determine the risk of recurrence is also often not feasible due to limited availability of such services and sociocultural and religious restrictions.[49,50]

Gaps in Provision of Fetal Screening and Diagnosis Services in Developing Countries

There are many factors that militate against the provision of effective fetal screening and diagnosis in developing

countries when compared with the more developed countries. These challenges mean that women often do not have the fetal screening options for pregnancy care that optimize outcomes. These deficiencies range from gaps in the provision of services and healthcare policies to a paucity of suitable imaging equipment, as well as the lack of appropriately trained pediatric surgeons, neonatologists, and perinatal pathologists. Even when these facilities exist, there are often limitations to access as a result of undeveloped transport and referral systems. We highlight some of the gaps in this section and recommend approaches for change.

Lack of a coordinated healthcare policy in relation to fetal medicine services

Most developed countries have standard policy recommendations regarding the provision of prenatal screening and diagnosis services. Such policies clarify and recommend minimum standards in respect of the provision of prenatal aneuploidy screening, fetal imaging, and the provision of safe pregnancy termination services. In most of these countries, all pregnant women are expected to have two or three routine US scans (one in each trimester), with additional scan services being provided for high-risk pregnancies.[51-53] Should a lethal or major fetal anomaly be detected, the option of termination of pregnancy is also available at different gestational age cut-offs, depending on the country.[48,54]

Prenatal US is sometimes requested by healthcare providers in the developing world, either as part of a routine baseline prenatal evaluation or for specific clinical indications evolving during the course of the pregnancy. However, opinions are still divided regarding the cost–benefit and rationale for routine prenatal US in a normal unselected population.[55] Some regulatory bodies do not support the routine use of US in a low-risk population.[56] In Nigeria, as an example of a country in sub-Sahara Africa, there are no national guidelines for prenatal screening, the request often being made on the initiative of the clinical care provider.[55]

Restrictive abortion laws and lack of abortion services.

Abortion laws are significantly more restrictive in most developing countries, where it is allowed only to save the woman's life. It is, however, often permitted on the grounds of lethal fetal anomalies in some of these countries. Whereas 84% of developed countries permit abortion due to fetal anomalies, only about 32% of countries in the developing region allow it.[57,58] Such restrictive legislation reduces the potential clinical and economic benefits of US screening for fetal anomalies in such countries.[59-61]

Low level of health education and lack of adequate antenatal care

In most of sub-Saharan Africa, only 30% of pregnant women in the urban areas have access to an obstetric US service, whereas in rural areas, this figure is estimated to be much less at about 6%,[42] similar to most other developing countries. This is because most women, especially those in the rural areas, are ignorant of the availability of prenatal screening for anomalies, some of the reasons being that they have limited access to adequate antenatal care and appropriate health education.[62] Some reports suggest that up to half of all pregnant women in LMICs do not have access to adequate antenatal care.[62] WHO and expert reports consistently highlight this lack of access to local, adequately resourced, healthcare facilities as an important reason for failed targets such as the Millennium Development Goals (MDG) 4 and 5, which were aimed to reduce child mortality by two-thirds and to improve maternal mortality by 75% by 2015, respectively.[62,63]

Most antenatal facilities in rural areas are under equipped, without prenatal imaging facilities, making them of little or no benefit to pregnant women. Even in some urban areas where these facilities are available, most women undergo imaging studies for reasons other than screening for anomalies. In a study conducted in the southern part of Nigeria, investigating reasons why women desire prenatal US, fetal viability was foremost, closely followed by gender determination among other reasons. None of the women mentioned prenatal diagnosis of fetal anomalies; this is likely to be largely due to their ignorance of the services,[52,55] as well as to sociocultural beliefs which do not allow or empower women to make decisions regarding their pregnancies.

Economic limitations on healthcare services: low gross domestic product and per capita expenditure on health

In most developing countries, little of the resources are usually committed to the health care of the people. Therefore, a pay-for-service health system is practiced making most health facilities to be beyond the reach of majority of the populace, especially the poorly educated and low-income parents.[2,56] For example, in Nigeria, according to the World Bank, the per capita government health expenditure was only 97 dollars in the year 2015 compared with 9,536 dollars in the United States.[64] Also only 4.16% of the total national budget in Nigeria was allocated to health in 2017, which was even <5.95% allocated in 2012.[65] The health expenditure of the Nigerian populace is out-of-pocket and unsupported by government funding in 95.34% of the population.[2] In contrast, in developed countries health care, including routine prenatal screening, is supported by health insurance schemes making it accessible and affordable for every pregnant woman.[2,16]

Lack of appropriate infrastructure in the rural areas

Practical and logistical considerations for suitability of US in a rural setting are very different to the urban setting. This is because many of the rural settings are remote, poorly accessible, and have unreliable water and electricity supply. For example, 80% of provincial African hospitals do not have conventional electricity supply making them inappropriate for setting up prenatal diagnostic centers.[51,57]

Most adequately equipped antenatal facilities are located in the urban areas, usually a significant distance away, making it difficult for women in the rural areas to access them. This nonaccessibility is usually due to inadequate roads and expensive transportation. Even where adequate roads are available, most people living in the rural areas are very poor and cannot afford the faster means of transportation. There are some reports suggesting that some women have to trek for about 3–4 h to get to the nearest facility, an exercise which could well be injurious to their health.[61-63]

Sociocultural and religious factors militating against fetal screening and diagnosis

In the developing countries, some studies suggest that some women, especially in the rural areas, do not attend antenatal facilities because of deeply held cultural beliefs and/or tribal traditions surrounding the nature of pregnancy and childbirth. Some believe that pregnancy disclosure could lead to unwanted religious or spiritual complications.[53,61,66] Some viewed pregnancy as a normal life event rather than a medical condition, therefore saw no reasons for antenatal care.[61]

In a study on the role of religion in decision making on antenatal screening for congenital anomalies, some faith did not consider congenital anomalies as a problem and did not consider termination to be an option in the case of the disabled fetus. Even though they support fetal screening, if the fetus has congenital anomalies, they believe that it is a sin to terminate "the life of an unborn child." Hence, severely malformed fetuses are allowed to be carried to term despite the parents' knowledge of the condition.[67,68] While this is a belief that is also held by many in developed countries, the potential benefit of antenatal detection of anomalies enabling parents and care-givers to tailor and plan postnatal care to optimize management of the condition when the baby is born is often lost to these belief systems. This is often due to the added problem of ignorance of options for mitigating the consequences of mismanaged care of the fetus born with congenital anomalies. For instance, antenatal detection of an anomaly will assist in making adequate planning and appropriate mode of delivery in a healthcare facility with optimal neonatal intensive care and pediatric surgical support.

The use of prenatal US in some countries is mainly for sex selection, which is having a negative impact on the affected societies. According to a Chinese proverb saying "it is a blessing to bear a son, a calamity to bear a daughter." The knowledge of the child's gender before birth has led to the abortion of many unborn daughters in some parts of the world, most notably in Asia, with significant imbalance in gender ratios.[57,69-73] This has informed the reticence of many healthcare planners to promote fetal anomaly screening because of the risk that surreptitious gender determination can lead to gender selection.[73]

Poverty of training opportunities and skilled manpower

US is the fundamental technique for prenatal diagnosis of malformations. Sensitivity and specificity of US for the detection of anomalies depend mainly on the training and expertise of the sonologists as well as the quality of the equipment used. Training in fetal anomaly screening requires much time and a lot of practice, close supervision and management, and extreme motivation.[42,52] One of the major challenges in developing countries is that of inadequate training opportunities as well as scarcity of trainers on fetal anomaly screening.

In a study by Adeleye *et al.*,[56] >90% of the prenatal US scans were performed in private facilities, and in >80% of cases, it was carried out by sonographers with questionable training and limited technical capability. Prenatal detection of abnormalities was only made in 14% of cases and these were mostly by trained sonographers. Furthermore, most of these were diagnosed in the late third trimester when termination of pregnancy was no longer an option in those practice settings. Consequently, intrauterine diagnosis of congenital anomalies is hardly ever made in these settings owing to the inadequacy of training of the sonographers.[56,72]

Use of poor-quality equipment/inadequate training on newly purchased equipment

Although US is becoming more available in resource-limited settings, the cost of purchase, technical skills required for maintenance, and user-dependent accuracy have limited its application in these settings.[74]

Due to limited resources, especially in the rural areas, outdated refurbished machines are usually purchased and this leads to generation of very low-quality images, which may also be contributing to the low detection rate of fetal anomalies.[52,57]

In settings where new US machines are purchased, they are usually purchased without making provision for operator training and maintenance. No technique is worthwhile

without appropriately trained specialized operators. Training on the equipment is at least as important as the proper choice of equipment. The WHO scientific group has stressed in its report, the need for appropriate training for general practitioners and specialists meant to use US. To optimize the use of such equipment, a sonographer or sonologist should be trained on the same type of machine that he is going to use in routine practice.[74]

Also, because of lack of maintenance culture in most developing countries, the quality of US images deteriorates with use, thereby limiting the detection of fetal anomalies.[42,57] Most pieces of equipment are purchased with little or no service and maintenance contracts, such that they are abandoned for relatively trivial faults which would have been amenable to easy repair with appropriate maintenance contracts.

Lack of ancillary services

The ability to make complicated fetal diagnosis is a waste if no clinician or facility to treat the patient is available.[52] There are no standardized guidelines for the management of prenatally diagnosed fetal anomalies in most developing countries. The provision of an US service must always be coupled with appropriate means of improving the management of the scan outcome. These will include the availability of services and specialists in genetics, neonatal intensive care, pediatric surgery, specialist nursing, and midwifery and perinatal counseling. In settings where these services are not available, there should be provision for transfer of a high-risk pregnancy to a regional obstetric center where the services are available. Furthermore, in the instance where lethal or severe fetal anomalies are detected, there should be access to safe abortion.[48] In these settings, access to facilities that will provide empathic care can make what would otherwise be a very difficult and sad birth experience more bearable for affected families.

Recommendations for improvement in the developing countries

The changes required need to be implemented at national, local, and professional levels. These will require addressing manpower, equipment, and infrastructural challenges.

At the national level, there is a need for the development of a low-cost policy for the provision of fetal imaging services. The need for this has been suggested by several previous reports, including position papers by the WHO[74] as well as several published articles[52] that highlighted the lack of a referral system. Such a policy will need to be underpinned by a health economic assessment that promotes low-cost technologies for imaging rather than technologies which low-resource countries cannot afford or maintain.[42] The policies should also be such that will inform local guidelines and referral pathways and these need to be well resourced to enable implementation.

A national or regional policy for fetal prenatal screening needs to be underpinned by regional fetal referral networks, which provide care services at primary, secondary, and tertiary levels. A culture of multidisciplinary team meetings across such networks will ensure that cross-disciplinary cooperation enhances the care that women and their families receive, as well as encourage minimum standards in quality of the service to be maintained by practitioners within the network. Such policies and practices will also engender a culture of service evaluation and clinical audit, often lacking in resource-poor settings.[75,76]

Given the issues of access to health care, there is an advocacy for imaging equipment such as US to be simple, portable, and handheld, minimizing the resources needed for servicing and maintenance.[42,57] For such policies to be effective, there is the need to stratify care such that fetal screening can be provided at primary, secondary, and tertiary levels so that fetal problems of increasing complexity can be referred to facilities that are appropriately staffed to enable triaging for optimum neonatal care.[52]

Given the fact that, there is a scarcity of appropriately trained US practitioners in developing countries, a program of training and certification will be required to ensure standards of practice relevant to the needs of the patients and communities. In this respect, collaborations between practitioners in established institutions in high- and low- resource countries will enable skills transfer to inform improvements. Such collaborations are also likely to enhance research and data acquisition regarding the scope and extent of the problems affecting care provision in resource-poor countries.[77,78] There are economic implications of promoting such skill transfer between institutions in developed and developing countries: active funding of such collaborations is, therefore, required by institutions requiring such skilled manpower, perhaps through funding support by institutions undertaking to provide such training, leveraging funding opportunities that present themselves through international donor agencies.[78-80]

There is also a need for low-resource countries to source and procure the imaging technologies that meet the crucial needs of fetal diagnosis in the local setting. For instance, countries where abortion services are only feasible for lethal anomalies may choose to invest in equipment that enable

the distinction of lethal from nonlethal anomalies, and the identification of major anomalies rather than the subtler anomalies are unlikely to profoundly affect postnatal care.[78,79] A coordinated approach to develop, promote, foster, and sustain fetal diagnostic services in resource-poor countries is now imperative.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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