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The oocyte paradox; a compelling cause for continued ART surveillance in a developing country

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Abstract

The introduction of assisted reproductive technology (ART) has revolutionised the management of infertile couples. ART is available in many developing countries, but only to those who can afford the service. This inequity in access has resulted in an unmet need amongst those who are economically vulnerable. Late presentation is common in developing countries due to the enormous cost of ART, resulting in a disproportionately larger cohort of older women seeking ART. Oocyte donation is in high demand in many developing countries, but there is often a lack of regulations and enforcement capabilities. This may inadvertently subject the oocyte to the law of supply and demand with consequent exploitation. Altruistic gamete donation has gradually been superseded by compensated donation, paving the way for commercialisation in contrast to the concept of 'a true gift'. The value of the human oocyte becomes a function of its designation either for research or treatment during ART.

In many developing countries where research in human reproduction is minimal and altruistic donation extremely low, the oocyte paradoxically attains a commercial status and is available to the highest bidder. There is a compelling need to strengthen regulatory agencies in developing countries to discourage the commodification of gametes. An important strategy involves the development of policies and guidelines for donor compensation rather than the current practice of discretion. Gamete sharing will reduce the pressure on ART recipients and, if properly implemented, will minimise desperation and discourage exploitation. In developing countries, Oocyte banking should be explored to allow equitable distribution of scarce gametes.

Keywords: *ART*; *developing country*; *oocyte*; *paradox*; *surveillance*

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The oocyte plays a vital role in human reproduction, and the determination of embryonic competence and outcome of assisted reproduction is hinged on the quality of the oocyte [1]. Oocyte quality is known to depend on the nuclear and mitochondrial genome alongside the microenvironment of the ovary [1]. The mammalian oocyte was first described by Karl Ernst von Baer in 1826 [2], and since then, research has mainly focused on understanding embryogenesis for fertility enhancement. The success of sperm-oocyte interaction depends on the competence of the oocyte [1, 2], thereby making the oocyte not just an integral part of reproduction but a crucial determinant of successful fertility outcomes.

The female reproductive lifespan depends on the number of primordial follicles and their survival throughout the individual's reproductive years [3]. At birth, a female foetus has about 20% of the original primordial follicles because of marked attrition in utero [4]. The oocyte remains in the meiotic prophase arrest until puberty, when a cohort of oocytes is cyclically recruited, with a few attaining maturity. Most of the recruited oocytes undergo atresia, reducing ovarian reserve as time goes by. It has been demonstrated that germ cells enter meiosis in a production line [5], and that the first cells to commence meiosis during foetal oogenesis are the first to ovulate in adult life [6]. The implication is that older women produce oocytes that have traversed more cell cycles during foetal oogenesis and are at greater risk of attrition of telomeres [6, 7]. Maternal age, therefore, is an important predictor of oocyte quality and capacity for successful embryonic

development [8]. With advancing maternal age, the ovarian response to oocyte stimulation is reduced and this ageing process affects the quality and quantity of available oocytes, contributing significantly to the decline in fecundity [9]. There has also been a global increase in the number of women delaying conception beyond the mid-thirties when fertility is known to decline from a combination of factors including chromosomal disorders, especially non-disjunction, resulting in higher miscarriages [9, 10].

Infertility is estimated to affect 8–12% of couples globally [11]. However, this figure is higher in many developing countries where poverty is endemic and access to advanced fertility management is far from equitable [12]. In many developing countries with low per capita income where funding for assisted reproductive technology (ART) is provided out of pocket, there exists an unmet need and consequent inequity in access to ART services, which is mainly available to those who can pay [12]. Most fertility centres in Nigeria are privately owned and do not have a uniform standard of practice. With late presentation being a common feature, the need for donor gametes, particularly oocytes, becomes imperative [13], necessitating robust policies, guidelines and enforcement to regulate clinical practice and prevent exploitation.

Sources of donated oocytes

Four broad categories of oocyte donors have been described in the literature and are classified as Occasional, In Vitro Fertilisation (IVF), Related and Professional donors [14, 15]. Occasional donors are unrelated individuals who spontaneously donate oocytes or who, on certain occasions, such as during tubal ligation, are willing to donate, knowing they have no further need for their oocytes. This type of donation has the advantage that the donor is healthy and fertile. However, it is rarely practised due to its poor acceptance, evidenced by a high refusal rate from potential donors [15]. Many patients willing to embrace this mode of donation have been found to be psychologically challenged and are often motivated by a quest for self-recognition [15]. Occasional donors are almost non-existent in Nigeria and many developing countries, where altruism is very rare.

Patients undergoing IVF may be approached to donate their oocytes to an anonymous client as part of the egg sharing protocol [15]. This is often premised on the patient having sufficient oocytes for her treatment. This method is fraught with ethical concerns, especially related to consenting for the donation and, more importantly, remuneration for such donation. With the advent of gamete freezing and its wide availability, this type of donation has drastically reduced. It may only persist where cost sharing is envisaged for uninsured clients paying out-of-pocket, a reality in many developing countries.

Related donors are those recruited by the couple, usually from among their families. It has the advantage of maintaining genetic inheritance and eliminating the commercialisation of gametes. However, it may pose a significant challenge of psychological consequences for the child(ren) due to complicated family dynamics [15]. Professional donors, on the other hand, are paid to donate their oocytes. This practice, which is quite prevalent in the United States [15], is discouraged in many countries in Europe where regulations exist to ensure reasonable compensation for lost manhours and transportation [16]. This inadvertently makes recipient cycles unnecessarily tedious with longer waiting times, consequently encouraging cross-border reproductive care [17, 18].

Oocyte cryopreservation

ART involves superovulation following gonadotrophin administration. The resultant follicles are monitored with the aid of a transvaginal ultrasound scan. At oocyte maturation following the administration of human chorionic gonadotrophin, a transvaginal ultrasound-directed oocyte retrieval (TUDOR) is performed. This process invariably results in the availability of supernumerary oocytes and embryos that can be frozen for future use.

Oocyte cryopreservation, often called 'female emancipation set in stone', is widely available in Europe and many developed countries [19]. It provides an opportunity for women with declining ovarian reserve and those needing chemotherapy to store their oocytes, which has been dramatically enhanced with the introduction of the vitrification technique [20, 21]. In countries where oocyte vitrification is available, its uptake has increased due to the desire of many women to delay motherhood either for social reasons or professional advancement, which unfortunately generates ethical concerns relating to cost-efficiency [21].

Medical indications for oocyte cryopreservation include conditions in which ovarian reserve is threatened, such as in women needing cytotoxic cancer treatment, genetic disorders such as mosaic Turner's syndrome and severe endometriosis. ART-specific indications for oocyte cryopreservation include treatment aimed at preventing ovarian hyperstimulation syndrome (OHSS), accumulating oocytes in poor responders, especially those needing preimplantation genetic diagnosis and more recently amongst female to male gender reassignment patients [22, 23]. Elective oocyte cryopreservation in many developing countries is not popular, and this has been attributed to poor awareness about its usefulness and availability [24, 25]. However, a registry review of ART in Africa between 2018 and 2019 suggested an increasing uptake of frozen embryo transfers (FET), which accounted for 23.1% of all treatment cycles [26].

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The oocyte paradox: research versus commercialisation in developing countries

Lutjen and colleagues in 1984, barely 6 years after the birth of the first IVF baby, reported conception in a 25-year-old lady with premature ovarian failure who had donor oocyte IVF treatment [27]. This indeed revolutionised the management of the infertile couple through the expansion of treatment options for female factor infertility. Deploying donor oocytes in IVF treatment effectively delineated factors affecting donated oocytes as distinct from those affecting endometrial implantation in the recipient [28]. This has encouraged research into various aspects of human reproduction, thereby widening the range of indications for IVF. Conception depends on the successful implantation of the embryo, which is premised on the interaction between a receptive endometrium and appropriate synchronisation of embryonic/endometrial development [28, 29]. Globally, the majority of donated oocytes derive from anonymous donors [30] whose interests, alongside those of the recipients, must be protected. Prioritisation of recipients in centres that practice routine oocyte cryopreservation is essential for fair allocation, and developing institutionalised criteria for recipient selection is critical, especially when oocyte demand far outweighs supply [30].

A review of ART practices amongst practitioners in Nigeria highlighted the need for the establishment of enforceable regulatory frameworks that should reflect local content, recognising and emphasising the peculiarity and context of developing countries [31]. This review, which looked at the ethical concerns related to IVF in Nigeria, documented challenges involved in oocyte donation, especially donor exploitation and denial of adequate information and counseling [31]. These moral concerns, they opined, resulted from poor ART regulation, and they charged the ethics committee of the Association for Fertility and Reproductive Health (AFRH) to urgently formulate ART practice guidelines for practitioners in Nigeria [31]. This is particularly important as the number of older women seeking IVF in Nigeria has been on the rise [32], and an unregulated environment in a low-income country is bound to fuel unscrupulous donor oocyte practices akin to gamete commercialisation.

Altruistic gamete donation is rare in Nigeria, where commercial donation is the prevailing practice [33], and this is akin to what is observed in many developing countries where poverty is an important motivating factor. Discontent about the donor oocyte reward system, suggestive of exploitation, has also been documented [33]. Where commercial oocyte donation exists, it has been opined that reimbursement should consist of fair compensation for inconveniences and risks suffered during the treatment [34]. This, however, is a challenge in many developing countries with poor ART regulations and standardised compensation schemes. The resultant effect is twofold: exploitation by the fertility centre or dishonesty by the oocyte donor seeking to donate only to the highest bidder, leading to oocyte commodification.

Research in human reproduction in many developing countries is minimal and in Nigeria, it is limited to preimplantation genetic testing of the embryo for monogenetic disorders especially sickle cell disease, which is prevalent in Sub-Saharan Africa [35]. Against this background of limited research, minimal altruistic donation, and increasing demand for donor oocytes by older women participating in ART, the oocyte in developing countries, paradoxically attains a commercial status and is invariably available to the highest bidder.

In Nigeria, feeble efforts have been made in regulating the practice of human reproduction. The AFRH, a non-partisan, non-governmental Association, has committed to developing guidelines for ART practice in Nigeria over the last two decades. AFRH has helped to create awareness about ART and has provided updates about reproductive health management to various health disciplines involved in ART. AFRH, however lack enforcement capacity and membership of the Association, is voluntary and as such, its guidelines are not binding on ART practitioners. There is therefore a compelling need to strengthen AFRH through collaboration with the Medical and Dental Council of Nigeria (MDCN), the regulatory body for doctors practising in the country. This partnership we opine will promote ethically sound ART practices through continued surveillance, data reporting and enforcement through appropriate sanctions. Furthermore, eliminating third-party agents who primarily exploit oocyte donors should be taken as a priority to prevent the consequent commodification of human gametes.

An essential strategy against commodification is the development of policies and guidelines aimed at streamlining and standardising donor compensation for both direct and indirect expenses incurred during the treatment cycle. This will invariably minimise indiscretions by individual ART facilities. Revisiting gamete sharing protocols, especially in the event of scarcity, will reduce the pressure on ART clinics and recipients, reducing desperation and discouraging exploitation. Emphasis must be placed on limiting oocyte donation to six attempts per donor in line with expert recommendations over concerns about the cumulative risks of severe adverse events rising as high as 13–36%. Health risks following oocyte donation include procedural complications such as intraperitoneal haemorrhage, pelvic infection, OHSS, ovarian torsion and idiosyncratic reactions to anaesthetic agents used during the procedure. Others include loss of anonymity, psychological risk, which may present as donor regret or ambivalence over the procedure and the possibility of diminished ovarian reserve [36, 37].

Investing in oocyte banking services, which have the advantage of reducing recipient waiting period, enhancing oocyte/endometrial synchronisation and allowing quarantine measures while still retaining similar fertilisation, implantation and pregnancy rates [38, 39], should be the next step in developing countries, particularly Nigeria. However, this must be approached carefully, considering ethical principles that govern the intake, storage and distribution of stored oocytes [40].

Conclusion

There is an increasing demand for the use of donated oocytes in Nigeria, as evidenced by a growing number of older women seeking IVF. This has resulted in relative oocyte scarcity and, against the background of poverty, weak regulatory frameworks and poor enforcement, may tilt the practice in favour of commodification. Enhancing the enforcement capacity of regulatory bodies through surveillance and requisite sanctions, while promoting gamete sharing where applicable, will provide critical short-term measures to discourage the commercialisation of human gametes. Exploring the option of establishing oocyte storage banks will address the issues related to equity and fairness in the allocation of oocytes, thereby discouraging availability to the highest bidder. The value of research in human reproduction cannot be overemphasised, and it is pertinent that developing countries pay attention not only to the client service aspect of reproductive health but also to expand the horizon of locally relevant research in ART.

Conflict of interest

The authors report no conflict of interests.

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