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HIV Infection, Combined Antiretroviral Therapy, and Female Infertility in Sub-Saharan Africa: Implications for Assisted Reproductive Technology Access

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Abstract: **Background:** Human immunodeficiency virus (HIV) infection disproportionately affects women in Sub-Saharan Africa (SSA) and is associated with reduced fertility through complex biological, endocrine and behavioural mechanisms. Despite the widespread rollout of combined antiretroviral therapy (cART), HIV-positive women continue to experience significantly higher rates of infertility compared to HIV-negative counterparts. Assisted reproductive technology (ART) represents the definitive treatment for tubal-factor infertility, the most prevalent cause of infertility in this population; however, access remains critically limited across the SSA region. **Objective:** To systematically review the published literature examining the relationship between HIV infection, cART use, and infertility in SSA women of reproductive age, and to assess the availability, accessibility, and outcomes of assisted reproductive technology in the region. **Methods:** A comprehensive search of published and grey literature from 2012 to 2022 was conducted across six databases including MEDLINE, PubMed Central, Cochrane Library, Google Scholar, Meta-Register of Controlled Trials, and the Networked Digital Library of Theses and Dissertations. After screening 2,569 records, 47 studies meeting pre-specified inclusion criteria were included for thematic analysis. **Results:** Six major themes emerged: (1) a persistently high burden of HIV infection among SSA women; (2) substantial cART coverage with incomplete fertility restoration; (3) regionally high rates of infertility with significant psychosocial consequences; (4) tuboperitoneal pathology as the predominant mechanism of HIV-associated infertility; (5) critical under-availability and unaffordability of ART services; and (6) major deficits in regional data reporting, which impede evidence-based policy formulation. **Conclusion:** HIV-positive women in SSA face a dual burden of infection and infertility compounded by limited access to reproductive care. Despite effective cART programmes, fertility does not fully normalise. Urgent policy action is needed to integrate fertility care into HIV management, establish public-sector ART services, and strengthen regional data surveillance systems.

Keywords: HIV; combined antiretroviral therapy (cART); female infertility; Sub-Saharan Africa; assisted reproductive technology; in vitro fertilisation.

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INTRODUCTION

Human immunodeficiency virus (HIV) infection remains one of the most consequential public health challenges of the twenty-first century, with a geographically unequal burden that falls most heavily on the Sub-Saharan African (SSA) region. By the end of 2021, approximately 20.6 million individuals in eastern and southern Africa alone were living with HIV, representing 53% of the global total [1]. The epidemic is distinctly feminised: among adults living with HIV globally in 2021, 53.7% were women aged 15 years and above, and in countries such as Botswana women constitute 56% of all persons living with HIV (PLHIV) [2].

The intersection of HIV and reproductive health in SSA has increasingly attracted scientific and policy attention. Substantial evidence indicates that HIV-positive women experience infertility at rates significantly exceeding those of their HIV-negative counterparts, driven by a complex interplay of direct viral pathophysiology, immunological derangement, endocrine disruption attributable to cART, and behavioural factors including avoidance of condomless intercourse [3, 4]. Infertility is defined by the World Health Organization (WHO) as the failure to achieve a clinical pregnancy after 12 or more months of regular, unprotected sexual intercourse [5]. Globally, the condition affects approximately 48

million couples and 186 million individuals of reproductive age.

The epidemiological co-occurrence of HIV and infertility creates a profound unmet need in SSA. Childbearing carries deep cultural significance across most SSA communities, and childlessness frequently precipitates social stigma, marital dissolution, financial hardship, and psychological morbidity for affected women [6, 7]. Despite this burden, fertility care — and assisted reproductive technology (ART) in particular — remains inaccessible to the vast majority of SSA women. Current ART coverage in Africa stands at less than 1.5% of the population requiring it [8], and Africa has the lowest number of ART cycles globally according to International Committee for Monitoring Assisted Reproductive Technologies (ICMART) data [9].

The transformative rollout of cART across SSA over the past two decades has substantially improved survival and quality of life for PLHIV and has been associated with some improvement in fertility outcomes. Many SSA countries have made remarkable progress towards the UNAIDS 95-95-95 targets — 95% of PLHIV diagnosed, 95% of those on treatment, and 95% achieving viral suppression by 2025 [10]. Nevertheless, the assumption embedded in the UNAIDS Spectrum model that women on cART for more than six months achieve fertility equivalent to HIV-negative women is not consistently supported by cohort data [3], underscoring the need for integrated reproductive health strategies.

This review synthesises available evidence on the burden of HIV-associated infertility in SSA women, the mechanisms through which HIV and cART impair fertility, the psychosocial consequences of infertility in this population, and the current status of ART availability and access. Its findings are intended to inform the formulation of evidence-based policies and programmes for safe, affordable, and equitable fertility care in the region.

METHODS

Study Design

A narrative literature review was conducted following established systematic search principles. Published and unpublished literature on the impact of HIV infection and cART on the fertility of SSA women, and on the role of ART in this population, was systematically identified and critically appraised.

Eligibility Criteria

Studies were eligible for inclusion if they reported on: (i) SSA women of reproductive age (18–49 years); (ii) HIV-positive women on cART; or (iii) women with infertility who had undergone ART in SSA. Both qualitative and quantitative study designs were accepted. Studies conducted exclusively outside SSA, or focused on causes of infertility unrelated to HIV infection, were excluded. Only English-language publications from 2012 to 2022 were considered, reflecting the contemporary cART era.

Search Strategy

Six databases were searched: the University of South Wales Library, Cochrane Library, MEDLINE, PubMed Central, Meta-Register of Controlled Trials, and the Networked Digital Library of Theses and Dissertations. The search strategy employed Boolean operators combining the following MeSH and free-text terms: ["HIV" OR "Human Immunodeficiency Virus"] AND ["subfertility" OR "infertility" OR "subfecundity"] AND ["antiretrovirals" OR "antiretroviral therapy" OR "ARV" OR "HAART"] AND ["female" OR "women"] AND ["Africa" OR "Sub-Saharan Africa"] AND ["ART" OR "IVF" OR "ICSI"]. Reference lists of included studies were hand-searched for additional relevant citations.

Study Selection and Quality Assessment

The initial search yielded 2,490 database records, supplemented by 79 records identified through grey literature and reference scanning. After duplicate removal, 2,062 records were screened by title and abstract, with 1,886 excluded for lack of relevance. Full texts of 176 articles were reviewed, and 47 met the final inclusion criteria. Quality assessment prioritised peer-reviewed publications in reputable journals; expert opinion pieces, editorials, and single case reports were excluded to minimise bias. Inclusion of exclusively open-access articles due to resource constraints represents a recognised limitation.

RESULTS

HIV Infection in Sub-Saharan Africa

HIV-1 is a ribonucleic acid retrovirus of the Lentivirus genus, transmitted via mucosal contact, parenteral inoculation, and vertically from mother to child [11]. Without treatment, progressive immunosuppression culminates in acquired immunodeficiency syndrome (AIDS). The SSA region carries the global epicentre of infection, with an average adult HIV prevalence of approximately 3.9%, dramatically exceeding global averages [1].

In 2021, the ten countries recording the highest national HIV prevalences were all located in SSA: Eswatini (26.8%), Lesotho (21.1%), Botswana (19.9%), South Africa (19.1%), Zimbabwe (11.9%), Namibia (11.6%), Mozambique (11.5%), Zambia (11.1%), Malawi (8.1%), and Equatorial Guinea (7.3%) [12]. Risk factors driving transmission are diverse and include early sexual debut, inconsistent condom use, multiple concurrent partnerships, intergenerational sexual relationships, and gender-based violence [13]. Young women and adolescent girls are disproportionately affected, a pattern perpetuated by structural gender inequalities and socioeconomic vulnerability [2].

Combined Antiretroviral Therapy Coverage and Outcomes

The WHO recommends cART as the cornerstone of HIV management for all PLHIV regardless of CD4 count [1]. In 2014 UNAIDS launched the 90-90-90 targets, subsequently revised to 95-95-95 by 2025 [10]. By 2020, approximately 73% of all PLHIV globally were on cART with the majority achieving viral suppression [12]. Most high-burden SSA countries have made substantial progress towards these benchmarks. Table 1 summarises national performance data for the ten highest-burden countries.

Table-1: Target Achievement by End of 2021 for High HIV-Burden SSA Countries

Country	% PLHIV who know their status	% PLHIV accessing treatment	% PLHIV on cART virally suppressed
Eswatini	93	91	89
Lesotho	92	81	79
Botswana	94	92	90
South Africa	94	74	67
Namibia	92	91	84
Zimbabwe	96	91	85
Mozambique	No data	No data	No data
Zambia	91	90	87
Malawi	93	91	85
Equatorial Guinea	51	41	No data

The use of cART has substantially improved life expectancy and quality of life for PLHIV and has been associated with renewed reproductive aspirations [14, 15]. However, long-term cART exposure is associated with emerging complications including cardiovascular disease and endocrine dysfunction, particularly pituitary dysfunction, that have implications for fertility [4]. While viral suppression eliminates horizontal transmission risk — encapsulated in the U=U (Undetectable = Untransmittable) principle [16] — the full restoration of fertility to HIV-negative levels has not been demonstrated.

Infertility in Sub-Saharan Africa

The prevalence of infertility in SSA exhibits marked regional heterogeneity. Reported rates range from approximately 9% in Gambia to 21.2% in north-western Ethiopia, 20–30% in Nigeria, and 11.8% among women in Ghana [6, 17]. WHO demographic data indicate that over 30% of SSA women aged 25–49 years are unable to achieve a subsequent pregnancy, reflecting a particularly high burden of secondary infertility [6]. The total fertility rate in SSA has declined from 5.26 children per woman in 2010 to 4.56 in 2020, partly attributable to improving contraceptive access and urbanisation [18].

Secondary infertility predominates in SSA and is largely attributable to sequelae of pelvic inflammatory disease (PID) from sexually transmitted infections including Chlamydia trachomatis, Neisseria gonorrhoeae, and HIV itself [19]. This epidemiological pattern means that tubal-factor infertility is the most common indication for ART in the region.

Mechanisms of HIV-Associated Infertility

HIV impairs fertility through overlapping biological and behavioural pathways [3]. Biologically, the virus and cART produce derangements across multiple endocrine axes. Yousef *et al*. [4] demonstrated that HIV infection and cART are associated with pituitary dysfunction manifesting as hyperprolactinaemia, abnormalities in follicle-stimulating hormone (FSH) and luteinising hormone (LH), and thyroid and adrenal dysfunction. Elevated prolactin levels — attributable to both the direct viral effect and cART — suppress gonadotrophin release, impairing ovulation. Dysregulated FSH and LH levels produce primary hypogonadism or functional hypothalamic hypogonadism depending on the anatomical locus of viral or opportunistic infection pathology.

Thyroid dysfunction is also prevalent in HIV-positive patients. High TSH — secondary to HIV infection or cART hepatotoxicity — results in hypothyroidism, while opportunistic infections producing sick euthyroid syndrome generate low TSH. Both conditions impair ovarian function and fertility [4]. Adrenal insufficiency arising from elevated ACTH production or glucocorticoid resistance further compounds endocrine-mediated infertility [4].

At the level of the upper genital tract, HIV infection is associated with markedly higher rates of tuboperitoneal pathology. A retrospective study of 178 infertile women in KwaZulu-Natal, South Africa found that 61.2% had abnormal hysterosalpingographic (HSG) findings, predominantly tubal pathologies (72.5% of abnormal results), with HIV-positive women demonstrating a significantly higher incidence of tubal disease [20]. In a comparative HSG study in Nigeria involving 2,200

women, HIV-positive patients exhibited uterine synechiae in 26% versus 9.6% in HIV-negative women, and tubal abnormalities (distal and proximal occlusion, hydrosalpinx) in 52% versus 26% [21]. Yahya *et al*. [22] found in a cross-sectional study in north-western Nigeria that 81% of seropositive infertile women had secondary infertility secondary to tuboperitoneal abnormalities, compared to lower rates in seronegative women.

Neoplastic complications of HIV — including primary CNS lymphoma, non-Hodgkin lymphoma, invasive cervical cancer, and Kaposi sarcoma — may invade the suprasellar region, compromising pituitary perfusion and causing pituitary apoplexy with resultant hypopituitarism [4]. Opportunistic infections including tuberculosis, cytomegalovirus, and cryptococcal meningitis further damage the hypothalamic-pituitary axis [4].

Behaviourally, HIV-positive women face a distinct set of barriers to conception. Fear of horizontal HIV transmission during unprotected intercourse, fear of vertical mother-to-child transmission, concerns about deteriorating health, and anticipation of premature death all contribute to avoidance of condomless coitus and consequent subfertility [3, 23, 24]. Social stigma from communities and healthcare providers exerts additional pressure, reducing health-seeking behaviour and access to preconception and fertility care [24].

Effect of cART on Fertility

The introduction of cART has been associated with a partial recovery of fertility in HIV-positive women through immune reconstitution and the resolution of HIV-associated wasting and endocrine derangement [3]. Several population-level analyses of demographic and health surveys have demonstrated modest reductions in HIV-attributable fertility differentials in settings with high cART coverage [3]. However, complete equalisation of fertility rates with HIV-negative women has not been consistently demonstrated.

Iyer *et al*. [25] prospectively followed HIV-affected couples in a safer conception cohort in South Africa between 2013 and 2017. They found that HIV-positive women on cART had a two-fold increased risk of subfertility compared to HIV-negative women, a differential that persisted even after more than two years of cART. Seroconcordant HIV-positive couples exhibited 78% higher rates of subfertility than serodiscordant couples on long-term cART. The authors concluded that cART does not fully restore fertility, attributing residual subfertility to chronic immunosuppression and potential cART-related gonadotoxicity.

Marston *et al*. [26] studied the effects of HIV infection duration on fertility in African cohorts prior to cART initiation, demonstrating that prolonged infection duration is independently associated with greater fertility reduction. A separate analysis of 49 SSA household surveys from 2003 to 2016 identified significant regional variation, with southern Africa showing smaller HIV-attributable fertility differentials than other SSA subregions, and urban areas experiencing less HIV-related infertility than rural settings [3]. High national cART coverage was associated with a small reduction in the HIV-related fertility differential.

Psychosocial Impact of Infertility on HIV-Positive Women

In most SSA societies, parenthood is central to individual identity, social status, and marital stability. Children are regarded as ensuring continuity of the family lineage and conferring social power and prestige. Childlessness consequently carries severe punitive consequences including divorce, abandonment, stigmatisation, verbal and physical abuse, and financial deprivation [6, 17, 27].

Women bear a disproportionate share of the social burden of infertility. Dierickx *et al*. [27] conducted a qualitative study in urban Gambia documenting that infertile women experienced pervasive social exclusion, emotional and physical abuse, and financial difficulties, with lower socioeconomic status amplifying the severity of stigma. Anokye *et al*. [7] similarly demonstrated high rates of anxiety and depression among infertile couples in Ghana, with relationship strain precipitating violence against women and withdrawal of financial support. Pratt *et al*. [23] described the compounding effect of dual HIV-related and childlessness-related stigma in rural Uganda, producing profound intersectional marginalisation.

HIV-positive women additionally face stigma from healthcare providers, who may hold negative attitudes towards the reproductive aspirations of PLHIV [28]. This dual stigma — from both HIV status and infertility — reduces health-seeking behaviour and further impairs access to care [17]. The financial costs are also significant: Lince-Deroche *et al*. [29] found that 75% of women accessing sexual and reproductive health services in Johannesburg incurred out-of-pocket costs, with some spending over 10% of household income on these services.

Assisted Reproductive Technology in Sub-Saharan Africa

The WHO recognises access to high-quality fertility care as a fundamental component of reproductive health rights [5]. Despite this, ART remains profoundly inaccessible across SSA. A systematic landscape analysis by Chiware *et al*. [8] reported that fewer than 1.5% of the African population requiring ART can access it. Botha, Shamley and Dyer [30] conducted a systematic review confirming low availability and

utilisation of ART in SSA, noting that approximately 80% of African countries had reported no data on ART provision.

The ICMART World Report 2018 confirmed that Africa has the lowest absolute number of ART cycles of any world region [9]. While the required benchmark to meet infertility needs is approximately 1,500 ART cycles per million population per year, Africa achieved only 87 cycles per million in 2010 (the earliest year for which regional data were available), with data reported by only three countries. Although there has been subsequent growth, the gap between need and provision remains enormous [9].

Dyer *et al*. [31] conducted a retrospective survey of ART activity across 13 African countries, identifying 40 ART centres that collectively reported 25,770 IVF cycles. Clinical pregnancy rates were 28.0% per oocyte aspiration in fresh non-donor IVF cycles, and 35.8% per intracytoplasmic sperm injection (ICSI) cycle. Pregnancy rates were significantly higher (57.3%) in women under 35 years. However, delivery data were available for only 56.1% of pregnancies, indicating a substantial loss to follow-up — a critical limitation for generating reliable outcomes data.

The barriers to ART provision are multifactorial. Financial cost represents the single most important barrier: most SSA countries are low-income, with high poverty prevalence, and public sector funding for ART services is almost universally absent [9, 32]. The majority of existing ART clinics are privately operated and thus inaccessible to most couples [33]. Infrastructure deficits, absence of skilled laboratory and clinical personnel, and lack of appropriate equipment further limit capacity [9]. Cultural and ethical concerns — including questions about legitimacy of offspring, polygyny, and religious objections — also affect acceptability, though evidence on acceptability is largely limited to Nigeria [8].

Importantly, evidence confirms that ART provision is feasible in public sector, low-resource settings in SSA. Orhue *et al*. [33] demonstrated that batch IVF treatment at a Nigerian university hospital produced acceptable clinical pregnancy rates at reduced per-cycle cost with a low complication rate, providing a proof-of-concept model for public-sector fertility care.

Efforts to integrate HIV management with reproductive health services are ongoing. Heffron *et al*. [34] outlined consensus recommendations from a WHO multidisciplinary workshop for comprehensive services combining HIV management, safe conception options, and fertility care. Safer conception programmes addressing serodiscordant couples, pre-exposure prophylaxis, timed condomless intercourse during peak fertility, and cART optimisation represent important evolving strategies.

DISCUSSION

This review confirms that HIV-positive women in SSA carry a dual and compounding burden: a persistently elevated risk of infertility relative to HIV-negative women, and severely limited access to the assisted reproductive services needed to address it. The predominance of tuboperitoneal infertility in this population — driven by immunosuppression-related susceptibility to pelvic infections — makes IVF and ICSI the most clinically appropriate first-line fertility interventions. This is consistent with the broader epidemiology of secondary infertility in SSA, in which pelvic inflammatory disease sequelae are the leading aetiological factor.

Antiretroviral therapy has undoubtedly transformed the lives of PLHIV in SSA. The region's progress towards the UNAIDS 95-95-95 targets is commendable, and the partial fertility recovery associated with cART is clinically meaningful. However, the evidence reviewed here is consistent in demonstrating that cART does not fully normalise fertility [3, 25]. The residual deficit is likely multifactorial, reflecting ongoing chronic immunosuppression, cART-associated gonadotoxicity and endocrine disruption, persistent structural damage to the reproductive tract, and the behavioural suppression of condomless intercourse. Clinicians should therefore counsel HIV-positive women seeking pregnancy that cART initiation, while important, may not resolve fertility impairment and that specialist fertility evaluation is appropriate.

The psychosocial dimensions of infertility in HIV-positive SSA women deserve particular emphasis. The intersection of HIV-related stigma and childlessness-related stigma creates a uniquely isolating and harmful experience that affects physical safety, mental health, and economic security [23, 27]. Strategies targeting integrated HIV and fertility care must include components addressing stigma reduction, healthcare provider attitudinal reform, community sensitisation, and mental health support. Without these, biomedical interventions will remain inaccessible or underutilised.

The ART access gap in SSA is not primarily a clinical problem but a structural one. The concentration of ART services in private clinics, the near-total absence of public funding, infrastructure inadequacies, and the scarcity of trained reproductive medicine specialists collectively perpetuate inequity. Orhue *et al*. [33] demonstration that batch IVF in a public hospital setting is both feasible and cost-effective provides an important template. Regional health authorities and governments should explore batch IVF models, cross-subsidisation strategies, and regional task-shifting frameworks as practical pathways to expanding public-sector ART provision.

The deficit in regional ART data is a serious impediment to evidence-based policy. The observation

that approximately 80% of SSA countries have no ART data [30], and that nearly 44% of achieved pregnancies were lost to follow-up in the only pan-African ART registry study available [31], reflects systemic weaknesses in health information infrastructure. All countries with ART activity must commit to participation in the African ART registry, adhere to ICMART reporting standards, and invest in robust patient follow-up systems. Without reliable data, neither the true extent of unmet need nor the effectiveness of interventions can be accurately assessed.

Prevention also remains an indispensable element of any comprehensive strategy. Reducing HIV incidence, promoting early STI diagnosis and treatment, encouraging health-seeking behaviours, and integrating STI management with antenatal and reproductive health services would reduce the incidence of tuboperitoneal infertility upstream, thereby reducing demand for expensive and scarce ART services. Integration of preconception counselling into HIV clinic services represents a relatively low-cost intervention with high potential impact.

CONCLUSION

HIV-positive women in Sub-Saharan Africa experience significantly elevated rates of infertility compared to the general population, primarily due to tuboperitoneal pathology, HIV-related endocrine dysfunction, and behavioural impacts of living with HIV in stigmatised environments. While cART has meaningfully improved fertility outcomes, it does not fully restore fertility equivalence with HIV-negative women. The psychosocial consequences of infertility — compounded by dual HIV and childlessness stigma — are severe and wide-ranging. Access to assisted reproductive technology, the definitive treatment for tubal-factor infertility, remains critically inadequate across the region, constrained by cost, absence of public funding, infrastructure deficits, and scarcity of skilled providers.

Evidence-based policy action is urgently needed to: integrate fertility assessment and care into HIV management programmes; establish or expand public-sector ART services using cost-effective models; formulate national policies and clinical guidelines for fertility care in HIV-positive individuals; strengthen regional ART surveillance and data reporting; reduce stigma through community sensitisation and healthcare provider training; and invest in STI prevention to reduce the burden of tuboperitoneal infertility at source. The reproductive rights of HIV-positive women — globally recognised as a fundamental human right — cannot be realised without sustained, equity-oriented commitment from governments, health systems, and international partners.

RECOMMENDATIONS

Based on the evidence synthesised in this review, the following recommendations are made:

- Health ministries across SSA should formulate and implement national policies explicitly recognising fertility care as a component of universal health coverage, with dedicated public funding mechanisms for ART services.
- HIV treatment programmes should incorporate routine fertility assessment, preconception counselling, and referral pathways for infertility management as standard elements of comprehensive HIV care.
- Batch IVF and cost-subsidisation models should be piloted in public tertiary hospitals across SSA, drawing on the precedent established in Nigeria, with rigorous prospective data collection.
- SSA countries with ART facilities should achieve full participation in the African ART registry and comply with ICMART reporting standards; patient follow-up systems require urgent strengthening.
- Stigma-reduction interventions targeting both HIV and infertility should be embedded in community health programmes, and healthcare providers should receive training in non-judgemental, affirming care for PLHIV seeking fertility services.
- Research programmes should prioritise investigation of cART-associated gonadotoxicity mechanisms, optimal fertility preservation strategies for newly diagnosed HIV-positive women, and cost-effectiveness analyses of public-sector ART models in low-resource SSA settings.

Strengths and Limitations

This review addresses a clinically significant and policy-relevant topic, employing a systematic and rigorous search strategy across multiple databases. The inclusion of both qualitative and quantitative study designs provides a comprehensive perspective on the biomedical and psychosocial dimensions of the subject.

Several limitations should be acknowledged. First, the review is restricted to open-access literature; articles requiring purchase were excluded due to resource constraints, potentially introducing selection bias. Second, data heterogeneity precluded formal meta-analysis, limiting quantitative synthesis. Third, the absence of ART outcome data from most SSA countries means that conclusions regarding ART utilisation and outcomes rely on data from a small number of reporting countries — primarily South Africa and Nigeria — which may not be representative of the broader region. Fourth, loss to follow-up in the primary studies identified limits the reliability of outcome data. These limitations should be addressed in future systematic

reviews with prospective registration and access to comprehensive multi-country data.

DECLARATIONS

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