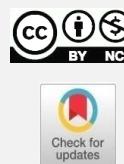


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**REVIEW ARTICLE****INTERSECTING PATHWAYS: THE COMPLEX RELATIONSHIP BETWEEN HIV AND FERTILITY IN WOMEN WITH SICKLE CELL DISEASE****Emmanuel Ifeanyi Obeagu<sup>1,2</sup> , Chukwuma J. Okafor<sup>3</sup> **<sup>1</sup>Department of Biomedical and Laboratory Science, Africa University, Mutare, Zimbabwe.<sup>2</sup>Department of Molecular Medicine and Haematology, Faculty of Health Sciences, Witwatersrand, Johannesburg, South Africa.<sup>3</sup>Department of Pathology and Biochemistry, State University of Zanzibar, Tanzania.**Article Info:****Article History:**

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**Abstract**

Women with both human immunodeficiency virus and sickle cell disease face distinct reproductive hurdles stemming from intertwined biological, pharmacologic, and psychosocial influences. Each condition separately affects fertility due to immune dysregulation, persistent inflammation, hormonal interference, and blood vessel issues, while their simultaneous presence intensifies these impacts. This narrative review examines the intricate connections between HIV and SCD in women, highlighting processes that influence ovarian function, fertility preservation, safe conception, and maternal-fetal results. Literature related to the topic was compiled from PubMed, Scopus, Web of Science, and Google Scholar, concentrating on research about fertility, reproductive endocrinology, management of hematologic and infectious diseases, and the effects of antiretroviral therapy and hydroxyurea. Global standards from the World Health Organization and the Centers for Disease Control and Prevention were included to frame clinical recommendations. HIV and SCD intersect via mechanisms such as oxidative stress, endothelial dysfunction, gonadal suppression, and chronic inflammation, resulting in reduced ovarian reserve, menstrual irregularities, and subfertility. Pharmacologic treatments, although crucial, may have cumulative gonadotoxic impacts, underscoring the necessity for fertility preservation methods. Multidisciplinary approaches that incorporate hematologic stabilization, optimization of ART, reproductive counseling, and strict adherence to PMTCT guidelines enhance reproductive results and lower the risk of vertical transmission. The convergence of HIV and SCD creates complex reproductive issues that necessitate personalized, evidence-based care. Timely preconception counseling, comprehensive clinical care, and focus on psychosocial elements are essential for maintaining fertility and safeguarding maternal and fetal health. Additional studies are necessary to clarify the lasting impacts of ART and hydroxyurea on ovarian reserve and pregnancy results.

**Keywords:** Fertility, HIV, reproductive health, sickle cell disease, women.

**INTRODUCTION**

The overlap of human immunodeficiency virus (HIV) infection and sickle cell disease (SCD) creates a distinct and increasingly important public health issue, especially in sub-Saharan Africa, where both diseases are prevalent. Every disease independently imposes a significant burden of morbidity and mortality; however, their simultaneous presence in women creates intricate interactions that reach beyond hematologic and immunologic areas to include reproductive and psychosocial well-being. This review investigates the combined effects of HIV and SCD on female fertility, analyzing mutual and synergistic biological mechanisms, clinical results, and public health

concerns<sup>1,2</sup>. Worldwide, around 38 million individuals are living with HIV, and nearly 300,000 infants are born each year with SCD, predominantly in Africa. In certain African nations, the HIV rate among women of reproductive age surpasses 10%, whereas the frequency of SCD traits varies from 10–40% based on geographic area. With enhanced treatment and early diagnosis increasing life expectancy, more women are living into their reproductive years with both conditions. This overlap in epidemiology emphasizes the need to focus on fertility, safe conception, and maternal outcomes in this population topics that have been historically overlooked in both hematologic and reproductive studies<sup>3,4</sup>.

HIV infection has diverse impacts on female fertility due to immune suppression, chronic inflammation, hormonal imbalance, and infections in the reproductive tract. Chronic viremia and immune activation can modify gonadotropin signaling, hinder ovarian folliculogenesis, and increase the risk of anovulation and menstrual irregularities. Moreover, antiretroviral therapy (ART) crucial for viral suppression can affect reproductive hormones and mitochondrial function, sometimes resulting in subfertility or early ovarian aging<sup>5,6</sup>. Similarly, SCD influences fertility via chronic hemolysis, tissue hypoxia, and vasoocclusive events that hinder blood circulation to reproductive organs. These pathophysiological injuries can result in ovarian ischemia, decreased follicular reserve, postponed menarche, and menstrual abnormalities. Women with SCD additionally face increased oxidative stress, potentially further impairing hormonal equilibrium and oocyte viability. The ensuing interplay of anemia, inflammation, and hypoxia can greatly hinder both natural conception and the maintenance of pregnancy<sup>7,8</sup>. When HIV and SCD are present together, their physiological processes overlap, leading to increased reproductive risks. Chronic inflammation, endothelial dysfunction, and oxidative stress are heightened, impacting not just ovarian reserve but also uterine receptivity and the potential for implantation. Additionally, pharmacological management becomes intricate: ART and hydroxyurea, essential for disease management, may have similar oxidative and cytotoxic impacts on ovarian tissue. These insufficiently studied drug interactions present possible dangers to fertility preservation and necessitate additional research<sup>9,10</sup>. Apart from biological factors, the sociocultural and psychosocial aspects of fertility in women with HIV and SCD are significant<sup>11,12</sup>. In numerous African cultures, fertility is a vital component of femininity, and infertility frequently results in stigma, unstable marriages, or emotional turmoil. Women with these ongoing health issues often encounter obstacles to reproductive guidance, assisted reproduction, and prenatal services. The stigma associated with HIV and inherited diseases exacerbates social isolation and restricts access to fertility services. The overlap of HIV and SCD thus signifies a medical intersection, as well as a reproductive and social crossroads that necessitates comprehensive approaches<sup>13,14</sup>.

The aim of this review is to explore the complex relationship between HIV and SCD and their combined impact on fertility in women.

#### **HIV and fertility in women**

The effect of HIV on women's fertility is an important research focus, as the virus can affect multiple facets of reproductive health. Research has consistently demonstrated that women with HIV encounter unique difficulties related to fertility, such as hormonal disruptions, changed menstrual patterns, and increased infertility risks<sup>15</sup>. The information provided demonstrates the influence of HIV infection on women's fertility, focusing on critical elements such as the effects of viral load, ART usage, and immune function on reproductive wellness. A significant observation from the empirical data is the link between

HIV and menstrual irregularities. Research by Kuete *et al.*<sup>16</sup>, revealed that women with HIV were more prone to menstrual irregularities than those without the virus. Women with elevated viral loads were more inclined to report irregular menstruation or amenorrhea. This is believed to result from HIV's direct impact on the hypothalamic pituitary gonadal axis, responsible for regulating the menstrual cycle.

Regarding ovulatory dysfunction, empirical studies confirm that HIV infection can directly affect ovarian function. Seidman and Weber discovered that women with HIV not receiving antiretroviral therapy (ART) faced an increased risk of ovarian dysfunction, as shown by higher follicle-stimulating hormone (FSH) levels, indicating diminished ovarian reserve<sup>17</sup>. Research by Heffron *et al.*<sup>18</sup>, indicated that HIV-positive women might undergo menopause earlier than their HIV-negative counterparts, possibly resulting from immune dysregulation and ongoing viral infection. These results indicate that HIV infection could hasten the natural reduction in reproductive ability, thus influencing fertility. Additionally, antiretroviral therapy (ART) has been found to impact fertility in HIV-positive women, although the evidence is inconsistent. Gambadauro *et al.*<sup>19</sup>, examined the impact of different ART regimens on female fertility, discovering that specific drugs, especially those in the nucleoside reverse transcriptase inhibitor (NRTI) category, are linked to metabolic changes such as weight gain, insulin resistance, and lipid modifications. These metabolic changes can affect fertility by disturbing the hormonal equilibrium needed for conception. In contrast, contemporary ART treatments, including integrase inhibitors, demonstrate fewer adverse impacts on reproductive health since they are less prone to induce metabolic issues. Nonetheless, there is a scarcity of long-term studies examining the impact of ART on fertility, and further investigation is required to thoroughly comprehend the long-term reproductive effects of ART in HIV-positive women.

Additionally, empirical evidence indicates that women with HIV have a higher likelihood of developing pelvic inflammatory disease (PID), a recognized risk factor for infertility. Research by Vetter *et al.*<sup>20</sup>, indicated that HIV-positive women experienced a greater occurrence of PID than HIV-negative women, probably due to the immune suppression attributed to the virus. PID can result in scarring of the fallopian tubes, which raises the likelihood of infertility and ectopic pregnancy. The heightened susceptibility to PID in women living with HIV is believed to be associated with modified immune responses that may hinder the body's capability to combat infections impacting the reproductive system. Alongside these biological aspects, empirical studies have also explored the psychological and social elements affecting fertility in HIV-positive women. Nazari *et al.*<sup>21</sup>, discovered that women with HIV experiencing stigma and discrimination were less inclined to pursue reproductive health services, such as fertility treatments. This stigma, along with the physical difficulties linked to HIV, may increase the obstacles women encounter in becoming pregnant. Social

support and access to counseling are essential elements of fertility management for women living with HIV, as they can alleviate the emotional and psychological strains linked to fertility issues<sup>21</sup>. Empirical research also emphasizes the significance of immune function in relation to fertility. Riddell *et al.*<sup>22</sup>, discovered that women with reduced CD<sup>4+</sup> counts (an important indicator of immune health) were more prone to face fertility problems, including delayed conception or miscarriage. This is believed to result from the immune suppression linked to HIV, which may alter the uterine environment, hinder embryo implantation, and heighten the risk of pregnancy loss.

#### Sickle cell disease and fertility

SCD, a hereditary condition marked by the formation of misshapen red blood cells, can greatly affect multiple organ systems, such as the reproductive system. Research has indicated that fertility in people with SCD, especially women, is affected by a mix of factors such as hormonal irregularities, organ impairment, and the impacts of long-term illness. This part examines empirical research that has investigated the connection between SCD and fertility, emphasizing important conclusions related to menstrual dysfunction, ovarian function, pregnancy results, and fertility treatments<sup>23-25</sup>. A major reproductive issue encountered by women with SCD is menstrual irregularities. Research indicates that women with SCD tend to have a higher likelihood of experiencing irregular menstrual cycles or early menopause than the general population. Greydanus *et al.*<sup>26</sup>, discovered that approximately 50% of women with SCD indicated menstrual irregularities, such as oligomenorrhea (infrequent menstruation) and secondary amenorrhea (lack of menstruation). This menstrual dysfunction is believed to arise from various elements, such as hormonal imbalance, persistent pain, and the direct impact of sickling on reproductive organs. Chronic anemia and hypoxia (reduced oxygen flow to tissues) can also lead to menstrual irregularities by disturbing the fragile hormonal equilibrium required for regular menstrual cycles.

Empirical data suggests that women with SCD might have diminished ovarian reserve and premature ovarian insufficiency. Silva *et al.*<sup>27</sup>, discovered that women with SCD exhibited elevated follicle-stimulating hormone (FSH) levels and reduced estradiol levels, both indicating a decreased ovarian reserve. The persistent inflammation and hypoxia associated with SCD may cause oxidative stress, which is believed to harm the ovaries gradually. Moreover, blood transfusions are crucial for treating SCD but can result in iron overload, potentially affecting ovarian function negatively. Ghafuri *et al.*<sup>23</sup>, discovered that iron accumulation from frequent blood transfusions was linked to reduced fertility potential in women with SCD, which further complicates their reproductive health. Empirical research on pregnancy outcomes in women with SCD has also indicated that fertility and pregnancy are strongly associated with disease severity. Women with severe types of SCD, like sickle cell anemia (SS), face an increased risk for complications during pregnancy, including preeclampsia, gestational diabetes, intrauterine growth

restriction (IUGR), and premature birth. Canelón *et al.*<sup>28</sup>, found that women with SCD had a higher likelihood of experiencing miscarriage and stillbirth than the general population.

Nonetheless, female individuals with SCD do not universally experience fertility issues, and numerous women with the condition are able to conceive and carry pregnancies to term, particularly when their condition is effectively managed. Johnson *et al.* found that women with stable SCD and effective clinical management had fertility rates similar to those of the general population, indicating that disease management significantly influences reproductive health. Effective handling of complications associated with SCD, like pain crises and anemia, can aid in maintaining ovarian function and enhancing fertility results. Moreover, progress in SCD management, including hydroxyurea and blood transfusions, has enabled many women with SCD to successfully complete pregnancies, although vigilant monitoring throughout pregnancy is crucial<sup>29</sup>.

The role of hormonal treatment in addressing fertility in women with SCD is another focus of interest.

Hormonal contraception and hormone replacement therapy (HRT) are frequently utilized to manage menstrual cycles and reduce symptoms of ovarian insufficiency in women with SCD. Morris *et al.*<sup>30</sup>, discovered that hormonal contraceptives, especially those based on progestin, effectively regulated menstruation and alleviated menstrual-related symptoms in women with SCD. The use of hormonal therapies in women with SCD must be approached with caution since specific contraceptive methods, like combined oral contraceptives, may elevate the risk of thromboembolic events, a recognized complication of SCD. As a result, alternative options such as progestin-only contraceptives or intrauterine devices (IUDs) could be favored in this group. Fertility preservation methods, including egg freezing or ovarian tissue cryopreservation, are increasingly being contemplated for women with SCD who may encounter lowered fertility due to the condition or its therapies. While empirical evidence regarding fertility preservation in women with SCD is scarce, Brunson *et al.* propose that cryopreservation may provide a viable alternative for women with SCD facing early ovarian failure or diminished fertility as a result of repeated blood transfusions or complications from the disease<sup>31</sup>.

#### Intersecting pathways: The impact of HIV and SCD on fertility

The relationship between HIV infection and SCD establishes a complex environment that significantly affects female fertility. Both conditions individually modify reproductive physiology; however, when they occur together, their impacts align at the molecular, vascular, and endocrine levels, resulting in amplified reproductive dysfunction. HIV leads to ongoing immune activation and continuous CD<sup>4+</sup> T-cell loss, interfering with the hypothalamic pituitary gonadal axis due to sustained inflammation and cytokine imbalance. Increased levels of tumor necrosis factor-alpha (TNF- $\alpha$ ), interleukin-6 (IL-6), and interferon-gamma (IFN- $\gamma$ ) disrupt gonadotropin releasing hormone (GnRH) pulsing and ovarian steroid

production, resulting in anovulation, luteal phase issues, and menstrual abnormalities. Simultaneously, women with SCD undergo frequent vaso-occlusive crises, hypoxia, and oxidative stress, which diminish pituitary responsiveness to gonadotropins and lead to hypogonadotropic hypogonadism<sup>32</sup>.

Oxidative stress serves as a common pathogenic pathway linking HIV and SCD. In HIV infection, the replication of the virus and the metabolism of antiretroviral drugs produce reactive oxygen species (ROS) that harm oocytes and granulosa cells. In SCD, persistent hemolysis liberates free heme and iron, provoking lipid peroxidation and mitochondrial impairment in ovarian tissue. These processes unify to hasten follicular atresia and diminish ovarian reserve<sup>33</sup>. Damage to mitochondrial DNA and the shortening of telomeres seen in both HIV-infected individuals and those with SCD might exacerbate premature ovarian aging and subfertility. Endothelial health is essential for proper ovarian blood flow and follicle maturation. HIV and SCD both disturb vascular balance by causing endothelial activation, reducing nitric oxide, and leading to microvascular blockages. In SCD, sickled red blood cells lead to ischemic damage in the ovarian microcirculation, whereas HIV-related endothelial dysfunction is influenced by viral proteins like gp120 and Tat, which promote leukocyte adhesion and inflammation in the blood vessels<sup>34</sup>.

Therapeutic intervention adds complexity to the reproductive environment. ART revitalizes immune response but can cause mitochondrial damage and metabolic changes that impact reproductive health. Hydroxyurea, essential in SCD treatment, enhances erythrocyte rheology and decreases vasoocclusive crises but might have cytostatic and genotoxic impacts on rapidly dividing ovarian cells. Recent findings indicate that the simultaneous administration of ART and hydroxyurea might increase oxidative stress and DNA harm, although information is still scarce. These interactions highlight the crucial requirement for longitudinal studies examining their joint effects on ovarian reserve, menstrual regularity, and fertility potential. Chronic anemia and hypoxia in SCD may hinder ovulation and damage endometrial receptivity, while HIV-associated wasting and malnutrition worsen hormonal imbalances. Moreover, repeated transfusions in SCD can lead to iron overload, which can further compromise gonadal function via oxidative pathways<sup>35,36</sup>.

The impact on fertility in women with HIV and SCD goes beyond just biological issues. Concerns regarding vertical transmission, misunderstandings about genetic inheritance, and the stigma associated with chronic illnesses frequently hinder reproductive desires. Women might refrain from pursuing fertility evaluations or stop treatment because of worries regarding teratogenic effects or the incompatibility of therapy with pregnancy. The mental burden fueled by societal pressures of motherhood intensifies reproductive anxiety, underscoring the necessity for combined psychosocial and fertility counseling<sup>37</sup>. The interconnected biological and psychosocial factors relating HIV and SCD to infertility require a

multifaceted strategy. Thorough reproductive care must include monitoring of ovarian reserve, guidance on fertility preservation, and integrated management of ART and hydroxyurea. Timely referral to reproductive endocrinology and hematology experts is essential for personalized preconception planning. Additionally, combining WHO and CDC recommendations on safe conception and mother-to-child transmission prevention (PMTCT) can improve results and guarantee reproductive freedom<sup>38</sup>.

### Clinical management of fertility in women with HIV and SCD

The clinical handling of fertility in women who have both HIV and SCD poses one of the most sensitive challenges in contemporary reproductive medicine. These women traverse a complicated biological landscape characterized by persistent inflammation, endothelial impairment, and hormonal imbalance, all of which work together to hinder reproductive capabilities. As a result, management approaches should extend beyond traditional reproductive care, incorporating hematologic stability, infection management, and psychosocial assistance within a multidisciplinary framework. Preconception counseling serves as the foundation of clinical management. As per the WHO and the CDC, attaining continuous viral suppression prior to conception is essential to reduce the likelihood of HIV transmission to both partner and child. Simultaneously, ensuring hematologic stability is crucial in SCD to avert vaso-occlusive crises, significant anemia, or infections that could complicate conception or early pregnancy<sup>39,40</sup>.

Pharmacologic management requires meticulous coordination between ART and hydroxyurea, the primary treatments for HIV and SCD respectively. Although ART has significantly enhanced survival rates and lowered vertical transmission, its prolonged usage can affect gonadal steroid production and mitochondrial function, consequently influencing ovarian reserve. Hydroxyurea, while successful in decreasing SCD crises and the need for transfusions, has possible cytostatic and gonadotoxic risks, particularly with long-term use<sup>41</sup>. For women wishing to conceive, the choice to either persist with or temporarily stop hydroxyurea should weigh the dangers of maternal vaso-occlusive issues against the possibility of gonadal recovery. Present data indicates that ART combinations with tenofovir, lamivudine, and dolutegravir provide a beneficial safety profile for women of reproductive age; however, ongoing pharmacovigilance is essential to track drug interactions and reproductive results. Fertility preservation is a developing but often overlooked component of care for women managing both HIV and SCD. The combined impacts of oxidative stress, ongoing inflammation, and drug exposure can hasten ovarian aging, highlighting the importance of timely reproductive planning. Methods like oocyte or embryo freezing, ovarian tissue preservation, and in vitro fertilization (IVF) can provide effective reproductive choices when managed with safe viral suppression and stable hematologic conditions<sup>42,43</sup>.

For individuals who achieve pregnancy naturally or with assistance, the management of pregnancy needs to be tailored specifically. WHO recommendations suggest a minimum of eight antenatal appointments for high-risk pregnancies, highlighting the importance of monitoring viral load, optimizing hemoglobin, and tracking fetal growth. Ongoing use of ART throughout pregnancy is essential for maintaining viral suppression and avoiding mother-to-child transmission (MTCT), whereas hydroxyurea is typically stopped unless the potential severe complications from SCD surpass the possible risks to the fetus. Supportive actions like folate supplementation, sufficient hydration, and infection prevention assist in minimizing pregnancy complications related to anemia or vaso-occlusion. Delivery planning must consider viral load status, using cesarean section only in situations where the risk of MTCT is still high<sup>44</sup>.

In addition to biomedical care, psychosocial and ethical aspects are essential in managing fertility. Women living with HIV and SCD frequently encounter stigma related to reproduction, as well as confusion and worry regarding pregnancy and parenting. Worries about passing on HIV or SCD to children may hinder fertility desires, while societal pressures regarding motherhood can heighten emotional turmoil. Incorporating mental health services, peer support initiatives, and culturally appropriate reproductive counseling into care pathways improves psychological health and supports informed reproductive decisions<sup>45</sup>. Collaborative efforts across multiple disciplines are essential for effectively managing fertility in this group. Collaborative actions between obstetricians, hematologists, infectious disease specialists, and reproductive health professionals can align care strategies, enhance conception timing, and maintain consistent disease management during pregnancy and after childbirth. Health policies must be modified to enhance access to fertility services in HIV and SCD clinics, guaranteeing that women obtain equitable and evidence-driven reproductive care<sup>46</sup>.

#### **Underexplored interactions between antiretroviral therapy, hydroxyurea, and ovarian reserve**

The concurrent use of ART for HIV management and hydroxyurea for SCD control introduces a complex pharmacologic landscape that may influence ovarian function and long-term fertility potential in women. While both therapies are life-extending and disease-modifying, their combined biological effects on the ovarian reserve remain largely under-investigated and insufficiently documented in existing literature.

#### **1. Mitochondrial and oxidative stress pathways**

ART, particularly nucleoside reverse transcriptase inhibitors (NRTIs), has been linked to mitochondrial DNA depletion and oxidative stress within ovarian tissue, potentially impairing folliculogenesis. Similarly, hydroxyurea though cytoprotective in reducing sickling and vaso-occlusive crises induces oxidative DNA damage and mild cytotoxicity in rapidly dividing cells, including granulosa cells within ovarian follicles. The simultaneous administration of these agents could therefore amplify oxidative stress, reduce oocyte viability, and accelerate ovarian aging<sup>47</sup>.

#### **2. Hormonal and endocrine disruption**

Long-term ART use has been associated with altered hypothalamic-pituitary-gonadal axis regulation, affecting luteinizing hormone (LH) and follicle-stimulating hormone secretion. Hydroxyurea, on the other hand, may disrupt gonadal steroidogenesis and reduce estradiol synthesis through its effects on bone marrow and erythropoietic activity. This dual interference may result in subclinical hypogonadism, menstrual irregularities, and diminished ovarian response, which are often overlooked in routine clinical monitoring<sup>48</sup>.

#### **3. Genotoxic and epigenetic implications**

Both ART and hydroxyurea have demonstrated potential genotoxic and epigenetic effects, influencing germline integrity and follicular DNA stability. While the clinical relevance of these findings in women remains uncertain, animal models suggest cumulative exposure could alter gene expression linked to follicular apoptosis and ovarian reserve depletion. These effects may be particularly significant in young women who initiate therapy early and continue through reproductive years<sup>49</sup>.

#### **4. Reversibility and clinical monitoring**

Current data on the reversibility of drug-induced ovarian suppression in women with HIV and SCD are scarce. Monitoring ovarian reserve markers such as anti-Müllerian hormone (AMH), antral follicle count, and FSH levels could help identify subfertility risk early in treatment. Periodic reproductive health evaluation should be integrated into chronic disease management to balance hematologic and virologic control with fertility preservation<sup>50</sup>.

#### **5. Research and clinical gaps**

Despite increasing survival among women with dual HIV and SCD diagnoses, prospective studies on the reproductive impact of combined ART and hydroxyurea therapy are lacking. Most existing evidence is extrapolated from isolated studies on either therapy alone. Future investigations should prioritize longitudinal assessment of ovarian function, stratified by treatment duration, drug class, and disease severity, to guide evidence-based reproductive counseling<sup>50</sup>.

#### **Incorporation of current WHO and CDC recommendations on safe conception and prevention of mother to child transmission**

Safe conception for women with both HIV and SCD requires a careful balance between reproductive intentions, maternal health stability, and prevention of vertical HIV transmission. Both the WHO and the U.S. CDC have issued evidence-based recommendations to guide healthcare providers in ensuring safe conception and maternal care in seropositive women, including those with co-morbidities such as SCD.

#### **1. Preconception counseling and health optimization**

WHO (2021) and CDC (2023) guidelines emphasize comprehensive preconception counseling as a cornerstone of safe conception in women living with HIV<sup>22,23</sup>. Before attempting conception, women should undergo:

- Viral load suppression through consistent ART, ideally achieving undetectable viral levels for at least six months prior to conception.

- Optimization of SCD control, ensuring stable hemoglobin levels, hydration, and reduced frequency of vaso-occlusive crises.
- Screening and management of co-infections, anemia, and nutritional deficiencies that could compromise fertility or pregnancy outcomes.

## 2. ART and treatment safety

Both WHO and CDC recommend the continuation of ART during conception and throughout pregnancy, prioritizing regimens with the best safety and efficacy profiles.

- Dolutegravir based regimens are now the preferred first-line therapy due to their potency and lower risk of neural tube defects compared to older agents.
- Efavirenz remains an alternative for women already stable on the regimen prior to conception.
- ART should be closely monitored for potential hematologic or hepatic interactions with hydroxyurea in women with SCD, as drug overlap may influence maternal hematopoiesis.

## 3. Safer conception strategies for serodiscordant couples

For couples in which one partner is HIV-positive, WHO and CDC recommend evidence-based assisted conception techniques and timed unprotected intercourse only when viral suppression is achieved. Additional recommendations include:

- Pre-exposure prophylaxis (PrEP) for the HIV-negative partner during conception attempts.
- Sperm washing and intrauterine insemination (IUI) where resources permit, to reduce transmission risk.
- Avoidance of conception attempts during acute illness or uncontrolled viremia in either partner<sup>28,29</sup>.

## 4. Prevention of mother-to-child transmission

The WHO 2021 consolidated guidelines emphasize that with effective ART and appropriate obstetric management, the risk of vertical transmission can be reduced to below 2%<sup>41,42</sup>.

Key preventive measures include:

- Early antenatal ART initiation or continuation.
- Regular monitoring of viral load throughout pregnancy and the postpartum period.
- Safe delivery practices preferably vaginal delivery unless cesarean section is indicated for obstetric reasons.
- Postnatal infant prophylaxis, typically using nevirapine or zidovudine, depending on maternal viral suppression status.

## 5. Integrating SCD Care with Reproductive Health Services

For women with both HIV and SCD, WHO recommends integrated chronic care models that link hematologic management with reproductive health and HIV services. Regular follow-up should address anemia correction, iron balance, and infection prevention<sup>45,46</sup>.

This integrative approach enhances maternal well-being, reduces perinatal complications, and supports reproductive autonomy key components of both

WHO's reproductive health strategy and CDC's global HIV prevention agenda.

## CONCLUSIONS

Women with both HIV and SCD encounter a distinct combination of challenges that intersect at biological, pharmacological, and psychosocial dimensions, impacting fertility and reproductive results. The overlapping processes of chronic inflammation, oxidative stress, hormonal imbalance, and vascular issues generate increased risks for reduced ovarian reserve, menstrual irregularities, and subfertility. Therapeutic measures such as ART and hydroxyurea are crucial for managing the disease but raise further concerns due to their possible gonadotoxic and metabolic impacts. Even with these difficulties, evidence-based and collaborative management can greatly reduce reproductive risks. This review emphasizes significant deficiencies in understanding, especially concerning the prolonged effects of combined ART and hydroxyurea treatment on ovarian reserve and pregnancy results. Future studies should concentrate on long-term research, assessments of drug safety, and personalized fertility treatments to enhance care for this expanding demographic.

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## AUTHOR'S CONTRIBUTION

**Obeagu EI:** conceived the idea, writing the manuscript, literature survey. **Okafor CJ:** editing, critical review. Final manuscript is checked and approved by both authors.

## DATA AVAILABILITY

Data will be made available on request.

## CONFLICT OF INTEREST

None to declare.

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