



RESEARCH ARTICLE

Sperm Quality in HIV-1 Seropositive Men under Antiretroviral Therapy at HIV Integrated Clinic of Dr. Ciptomangunkusumo Hospital, Jakarta, Indonesia

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Abstract

The effect of human immunodeficiency virus (HIV) infection on male fertility as assessed by sperm quality is still in controversy in various studies. On the other hand, HIV seropositive men who are stable under the influence of antiretroviral therapy (ARV) experienced an increase in quality and life expectancy that allow them to have offspring. This study aims to investigate the sperm quality of HIV seropositive men in Indonesia. In addition, this study also compared sperm quality in HIV seropositive men who were stable under the influence of ARV (case group) with HIV seronegative men (control group). Semen samples from HIV seropositive male patients at the HIV Integrated Clinic, Ciptomangunkusumo Hospital, Jakarta, Indonesia were collected and analyzed for sperm in the laboratory, including: volume, pH, concentration, motility, morphology and sperm vitality. Comparison of sperm quality between the two groups was analyzed using independent t-test and Kruskal-Wallis test. Significant decrease in sperm quality was shown in the concentration, percentage of progressive motility and sperm vitality ($p < 0.05$), among groups of HIV seropositive men under the influence of ARVs and HIV seronegative. HIV infection and ARV treatment reduce sperm quality, in Indonesia. Further research is needed to study the mechanisms underlying the negative effects of HIV and ARVs that lead to decreased sperm quality.

Keywords: *Male infertility, Human sperm, Sperm quality, HIV, ARV.*

Introduction

Human Immunodeficiency Virus (HIV) infection has infected approximately 40 million individuals in the world. HIV virus particles are known to exist in the male reproductive tract and affect fertility [1]. However, the management of HIV infection with the use of antiretrovirals (ARVs), there has been an increase in the quality and life expectancy of individuals.

Obviously, this is good news for serodiscordant couples with HIV seropositive men to have offspring. Sperm quality in HIV-1 seropositive men has been extensively evaluated. The potential impact of HIV-1 infection on sperm still contradicts several studies with different designs and showing

inconsistent results. HIV infection is reported to cause oxidative stress induced by HIV proteins. In addition, ARV drugs are also known to be toxic in the spermatogenesis process. However, the negative effects on sperm cells resulting from ARV therapy in the treatment of HIV seropositive men are still debated [2-3].

Therefore, this study conducted a comparative study and analysis of sperm quality in HIV seropositive men on ARV, compared with HIV seronegative men. The novelty of this study is the first research conducted in Indonesia and links the quality of sperm to the type of ARV and CD4 value.

Methods

This study has received approval from the research ethics committee of the Faculty of Medicine, University of Indonesia (FMUI) with the ethical number 458 / UN2.F1 / ETIK / PPM.00.02 / 2019. The study design was an exploratory study using a case-control design which was divided into 2 groups, namely HIV seropositive men (Case group) and HIV seronegative (Control group) which were conducted in Indonesia, between July until October 2020.

Patients

Thirty five HIV seropositive men who underwent ARV therapy at the Integrated Service Unit of HIV Ciptomangkusumo Jakarta, Indonesia were taken with inclusion criteria, namely reproductive age (18 - 50 years), routinely taking ARV until now and at least for 6 months, not accompanied by opportunistic infections (asymptomatic) and not undergoing antibiotic, antidepressant, and other medications.

Furthermore, controls were men of reproductive age who are proven to be fertile (have had at least 1 child or have a pregnant female partner) and are HIV seronegative which is proven after a rapid HIV test. Informed consents were obtained from all the men involved in this study.

Sociodemographic, Behavioural and Clinical Data

Sociodemographic, behavioural and clinical data of patients were recorded: age, consumption of toxic substances during the last 3 months, CD4 value, HIV viral load, and drugs of ARV.

Semen Analysis

Semen samples were collected from masturbation into sterile containers after at least 3-5 days of sexual abstinence, then processed in the laboratory. The samples were processed after the liquefaction process was carried out for 30-60 minutes. Sperm concentration and motility were analyzed

using Makler counting chamber, while sperm morphology using Papanicolou staining. The normal reference value of WHO 2010 was applied for sperm quality determination. (WHO, 2010)

HIV's Laboratory Test

CD4 was determined by flowcytometry (BD FACS Calibur Cytometer, Bioscience, USA), while HIV viral load by polymerase chain reaction (PCR) (Abbot Real Time HIV-1 Assay CE, Abbot Laboratories, USA).

Statistical analysis

Statistical comparisons were performed using the independent Kruskal-Wallis t-test to demonstrate a significant changes in sperm quality of HIV seropositive men with those who were HIV seronegative. Statistical analysis was performed with SPSS 20 version for Windows and was considered significant if $p < 0.05$.

Results

Patients' characteristics

Table 1 demonstrates the sociodemographic, behavioural and clinical characteristics of HIV seropositive men under the influence of ARV therapy.

Semen characteristics

In semen characteristics, the results obtained was a decrease in sperm quality in almost all sperm parameters, between the HIV seropositive men under the influence of ARV and the control group (Table 2). However, a significant decrease was found in the parameters of concentration, percentage progressive motile and vitality of sperm. ($p < 0.05$) (Table 2).

Sperm abnormalities

In addition to semen characteristics profile, the sperm abnormality such as oligozoospermia, asthenozoospermia, teratozoospermia and azoospermia was shown in HIV seropositive men. (Table 3).

Table 1: Sociodemographic and behavioural and clinical characteristics the HIV-seropositive men

	Mean	SD
Age (years)	38.6	5.91
Toxics (n)		
Tobacco	10	28.6
Alcohol	3	8.6
CD4 (cell/uL)	598	235.1
Viral load (n)		

Undetected	23	65.7
<40 cells	10	28.6
>40 cells	2	5.7
ARV combination type (n)		
NRTI + NRTI	27	77.1
NRTI + PI	8	22.9

Table 2: Semen analysis of the HIV-seropositive (case) and HIV seronegative (control) men

	Case	Control	p
	Mean (SD)	Mean (SD)	
Semen parameters			
Semen volume (mL)	2.4 (1.6)	2.4 (1.6)	0.911
pH	7.3 (0.2)	7.4 (0.2)	0.197
Sperm concentration (cells x 10 ⁶ /mL)	32.3 (22.7)	65.5 (35.5)	0.001
Progressive motile spermatozoa [a] (%)	36.9 (15.9)	65.3 (20.3)	0.0
Nonprogressive motile spermatozoa [b] (%)	14.5 (12.6)	11.1 (11.5)	0.282
Immotile [c] (%)	48.2 (21.6)	24.4 (18.7)	0.001
Sperm Morphology	2.8 (2.1)	4.5 (1.9)	0.005
Sperm Vitality (%)	44.4 (20.6)	72.5 (11.2)	0.005
HOS test (%)	29.2 (16.7)	48.3 (23.8)	0.01

Table 3: Sperm abnormalities in the HIV-seropositive (case)

	Seropositive HIV (%)
Normozoospermia	73.0
Oligozoospermia	21.6
Asthenozoospermia	34.2
Teratozoospermia	74.2
Azoospermia	5.4

Discussion

This study is the first study in Indonesia that investigate sperm quality in HIV seropositive men in stable ARV conditions. In this study, it was found that there was a significant decrease in sperm concentration and motility in the HIV seropositive male group compared with the control group ($p < 0.05$). This study is in line with the study by Bujan et al (2007) which found a decrease in semen volume and sperm motility in HIV-seropositive male patients under the influence of ARVs compared to a control group, namely fertile seronegative men [4].

Furthermore, the results of previous studies reported various changes in sperm in HIV seropositive male patients [5-14]. In addition, Pilatz et al (2014) and Savasi (2016) also found that in all HIV seronegative male patients under ARV therapy experienced a decrease in sperm parameters such as volume, concentration, progressive motility and normal morphology, according to the values in the WHO 2010 reference values [15-16].

Currently, there is no clear mechanism to cause this impaired sperm concentration and motility. However, there is the possibility of silent inflammation along the genital tract, although not always accompanied by an increase in the number of leukocytes in the semen. A correlation between increased leukocytes in semen and decreased motility

has been reported and is associated with increased production of ROS [17-19]. The decrease in sperm concentration and motility will greatly affect the success of oocyte fertilization, if the patient must undergo Assisted Reproductive Technology, especially Intra Uterine Insemination (IUI) [20]. In addition to the possibility of silent inflammation, a possible mechanism underlying the negative effect of ARV therapy on sperm disorders has been described by Carr et al. that ARVs are involved in a variety of metabolic and endocrine dysfunctions that can affect the function of the testicles, genital tract and sperm [21].

The theory of mitochondrial toxicity in sperm, which can inhibit the production of energy or ATP, thereby disrupting sperm motility [22]. Although recent data show that ARVs significantly reduce total sperm count and progressive motility and increase abnormal sperm morphology, these side effects are offset by the tremendous benefits of ARVs to restore immunity, reduce morbidity and mortality, and improve overall sperm characteristics, related to sperm count [23].

Presumably, efforts need to be made to reduce complications due to HIV infection and the negative effects of ARVs, especially on sperm quality. The results of this study are expected to be the basis for the

development of further management and therapy for the reproductive success for HIV-seropositive men under ARV therapy who want to have healthy offspring.

Conclusion

In Indonesia, the sperm quality in HIV seropositive men had decreased, even though the patient was found to be stable under the influence of ARVs. However, further research is needed to determine the mechanism of damage to sperm quality due to HIV infection and or ARVs.

Conflict of Interest

There were no conflicts of interest in this study.

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