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Serum Malondialdehyde Levels in HPV-Negative and HPV-Positive DNA Tests in Women Infected with HIV in a Tertiary Hospital in Nigeria

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ABSTRACT

BACKGROUND

Human immunodeficiency virus (HIV) infection and human papillomavirus (HPV) are two major global health concerns, particularly in sub-Saharan Africa. Both viruses have been associated with increased oxidative stress, which can be quantified by measuring serum malondialdehyde (MDA) levels.

AIM

Assessing Oxidative Stress: Malondialdehyde is a biomarker for oxidative stress, which can be elevated in conditions like HIV infection. By measuring serum MDA levels, the study aims to evaluate the degree of oxidative stress in women with HIV, comparing those with and without HPV co-infection.

Comparing MDA Levels in HPV Status: The study seeks to determine if there are significant differences in MDA levels between HIV-infected women who are HPV-positive and those who are HPV-negative. This could provide insights into the interaction between HPV infection and oxidative stress in the context of HIV.

METHODOLOGY

A total of 150 women with HIV infection who were yet to be commenced on highly active antiretroviral therapy (HAART) were enrolled, comprising 75 whom tested positive for HPV DNA and 75 tested negatives for HPV DNA test. Serum MDA levels were measured using spectrophotometry. This study employed a comparative cross-sectional approach, recruiting 150 women from LASUTH's gynaecology, colposcopy, and medical oncology clinics via convenience sampling. Fasting blood samples were collected with consent, and serum malondialdehyde levels were measured spectrophotometrically.

Data Analysis:

Data was analysed using statistical package of the social sciences SPSS version 29. Serum MDA levels between HPV-negative and HPV-positive groups were estimated. We also assessed the correlation between MDA levels and HPV

status using regression analysis. There was a significant difference in MDA levels between HPV-negative and HPV-positive HIV-infected women.

CONCLUSION

Exploring serum MDA levels as a potential biomarker for cervical cancer risk assessment holds promise for improving early detection and intervention strategies. By understanding the role of oxidative stress in cervical carcinogenesis and evaluating the utility of serum MDA, healthcare professionals can develop more effective screening programs and targeted interventions to mitigate the impact of cervical cancer on women's health globally.

INTRODUCTION

Human immunodeficiency virus (HIV) and human papillomavirus (HPV) infections represent significant public health challenges globally, particularly in resource-limited settings like sub-Saharan Africa [1,2]. HIV weakens the immune system, making individuals more susceptible to various infections and malignancies, including HPV-related diseases such as cervical cancer, anal cancer, and genital warts[3]. Both HIV and HPV infections have been implicated in increasing oxidative stress levels in affected individuals[4]. Oxidative stress, characterized by an imbalance between reactive oxygen species (ROS) production and antioxidant defense mechanisms, plays a crucial role in the pathogenesis of several diseases, including HIV/AIDS and HPV-related cancers [5].

Oxidative stress, characterized by the imbalance between reactive oxygen species (ROS) and antioxidant defenses, contributes to cellular damage and dysfunction. In cervical cancer, high-risk human papillomavirus (HPV) infection is a major risk factor [6]. HPV oncoproteins E6 and E7 promote oxidative stress, which may facilitate viral persistence and cervical carcinogenesis [7]. ROS-induced DNA damage, including oxidative DNA lesions like 8-hydroxy-2'-deoxyguanosine (8-OHdG), promotes genomic instability and oncogene activation, contributing to cervical neoplasia [8].

Antioxidants, both endogenous and dietary, play a crucial role in counteracting oxidative stress. However, the efficacy of antioxidant supplementation in preventing cervical cancer progression remains uncertain. Targeting oxidative stress pathways presents potential therapeutic avenues. Combining antioxidants with conventional treatments could enhance efficacy, while selectively targeting ROS-producing enzymes or modulating redox signaling pathways may inhibit cervical cancer cell proliferation [9].

Oxidative stress plays a significant role in HIV infection and highly active antiretroviral therapy (HAART) usage. It leads to biomolecular damage and contributes to neurodegeneration, leading to poor clinical outcomes in HIV patients. The chronic production of reactive oxygen species (ROS) induces oxidative stress, which is especially impactful in the brain due to its high lipid concentration [10]. Studies have linked oxidative stress to HIV-associated neurocognitive disorders (HAND), suggesting its potential as a biomarker for these conditions [11]. Manipulating oxidative stress and antioxidant-dependent pathways could offer novel strategies for HIV cure and improving patient outcomes.

Understanding the complex relationship between oxidative stress, HPV infection, and cervical carcinogenesis is vital for developing effective preventive and therapeutic strategies. Further research is needed to unravel mechanistic links and identify novel targets for intervention, ultimately reducing the burden of cervical cancer and improving patient outcomes.

Recent studies have investigated the association between serum malondialdehyde (MDA) levels and cervical cancer risk factors, including HPV infection, smoking, age, and hormonal factors [12]. While some studies suggest a positive correlation between serum MDA levels and HPV infection, conflicting results have been reported [13].

Despite promising findings, the clinical utility of serum MDA as a standalone biomarker for cervical cancer risk assessment remains uncertain. Integrating serum MDA measurement with existing screening modalities like HPV testing and cervical cytology may enhance risk stratification and early detection of high-risk individuals [14].

Recent evidence also suggests a correlation between serum MDA levels and cervical cytology findings, such as Pap smear results and histopathological diagnoses [2,15]. Women with abnormal cervical cytology often exhibit elevated MDA levels, indicating a potential predictive biomarker for cervical cancer risk stratification.2

Understanding the relationship between serum MDA levels, HPV infection, cervical cytology findings, and other risk factors has significant clinical implications for cervical cancer screening, prevention, and treatment. Further research is needed to validate these findings and translate them into clinical practice, ultimately improving outcomes in cervical cancer prevention and management.

In conclusion, oxidative stress emerges as a crucial factor in the context of HPV infection, cervical cancer development, and HIV-associated complications. Understanding the intricate interplay between oxidative stress, viral infections, and cellular responses holds promise for novel therapeutic interventions and improved clinical management in these challenging health domains [16].

PRIMARY OBJECTIVE

To evaluate the levels of serum malondialdehyde (MDA) in HIV-negative and HIV-positive patients with positive HPV DNA tests.

SECONDARY OBJECTIVES

To compare the serum MDA levels between HIV-negative and HIV-positive patients with positive HPV DNA tests.
To investigate the association between serum MDA levels and socio-demographic variables and use of contraceptives.

MATERIALS AND METHODS

Study Design and Participants:
This study employed a cross-sectional design and recruited participants from the outpatient clinics of LASUTH. A total of 150 women with HIV infection who were yet to be commenced on highly active antiretroviral therapy (HAART) were enrolled, comprising 75 whom tested positive for HPV DNA and 75 tested negatives for HPV DNA test.

Inclusion Criteria

Women living with HIV
Age range: 18-65 years
Confirmed positive HPV DNA test results
Confirmed negative HPV DNA test result
Ability to provide informed consent.

Exclusion Criteria

Patients with a history of cervical cancer or previous treatment for cervical dysplasia.
Patients with known autoimmune diseases or chronic inflammatory conditions.
Pregnant women.
Patients on immunosuppressive therapy.

INSTRUMENT OF STUDY

Demographic and clinical data were collected using standardized questionnaires. Blood samples were collected from each participant, and serum was separated by centrifugation for subsequent analysis of MDA levels.

Measurement of Serum Malondialdehyde Levels

Serum MDA levels were measured using the thiobarbituric acid reactive substances (TBARS) assay, a well-established method for assessing lipid peroxidation. In brief, serum samples were mixed with thiobarbituric acid (TBA) reagent and heated in acidic conditions to form a colored complex, which was quantified spectrophotometrically at an absorbance wavelength of 532 nm. MDA levels were expressed as nanomoles per milliliter (nmol/ml) of serum.

Statistical Analysis

Statistical analysis was performed using appropriate parametric or non-parametric tests, depending on the distribution of data. The Student's t-test was used to compare continuous variables between groups, while categorical variables were analyzed using the chi-square test. A p-value < 0.05 was considered statistically significant.

RESULTS

Table 1: Socio-demographic variables

Variable	HPV negative	HPV positive	Total	X^2	P value
Age (years)					
21-30	3(4.0)	14(18.7)	17(11.3)	13.058	0.011
31-40	35(46.7)	21(28.0)	56(37.3)		
41-50	24(32.0)	26(34.7)	50(33.3)		
51-60	11(14.7)	14(18.7)	25(16.7)		
61-70	2(2.7)	0(0.0)	2(1.3)		
Mean age (Mean±SD)	42.61±8.10	41.15±9.60	41.88±8.88	t =1.011	0.314
Level of education					
Primary	10(13.3)	2(2.7)	12(8.0)	18.184	0.000
Secondary	34(45.3)	17(22.7)	51(34.0)		
Tertiary	31(41.3)	56(74.7)	87(58.0)		
Marital Status					
Single	7(9.3)	16(21.3)	23(15.3)	5.914	0.116
Married	66(88.0)	59(78.7)	125(83.3)		
Divorced	1(1.3)	0(0.0)	1(0.7)		
Separated	1(1.3)	0(0.0)	1(0.7)		

Variable	HPV negative	HPV positive	Total	X^2	P value
Lifetime number of sexual partner					
1	35(46.7)	20(26.7)	55(36.7)	19.994	0.000
2-3	35(46.7)	28(37.3)	63(42.0)		
More than 3	5(6.7)	27(36.0)	32(21.3)		
Age married					
15-20	7(10.3)	3(5.1)	10(7.9)	6.572	0.087
21-25	27(39.7)	14(23.7)	41(32.3)		
26-30	18(26.5)	26(44.1)	44(34.6)		
>30	16(23.5)	16(27.1)	32(25.2)		
Mean age (Mean±SD)	27.07±5.63	27.81±4.33	27.42±5.06	t=0.821	0.413
Age delivery (n=70)					
15-20	2(2.9)	5(9.3)	7(5.7)	8.830	0.032
21-25	23(33.8)	8(14.8)	31(25.4)		
26-30	19(27.9)	24(44.4)	43(35.2)		
>30	24(35.3)	17(31.5)	41(33.6)		
Mean age (Mean±SD)	28.54±5.62	28.93±5.45	28.71±5.53	t=0.378	0.706
Parity					
0	7(9.3)	21(28.0)	28(18.7)	16.092	0.007
1	11(14.7)	14(18.7)	25(16.7)		
2	22(29.3)	13(17.3)	35(23.3)		
3	25(33.3)	19(25.3)	44(29.3)		
4	8(10.7)	2(2.7)	10(6.7)		
5	2(2.7)	6(8.0)	8(5.3)		
Variable	**HPV negative**	**HPV positive**	**Total**	X^2	**Pvalue**
Awareness of contraception					
Yes	68(90.7)	75(100.0)	143(95.3)	7.343	0.007
No	7(9.3)	0(0.0)	7(4.7)		
History of use of contraception					
Yes	47(62.7)	55(73.3)	102(68.0)	1.961	0.161
No	28(37.3)	20(26.7)	48(32.0)		
Variable	**HPV negative**	**HPV positive**	**Total**	X^2	**Pvalue**
Smoke cigarette					
Yes	3(4.0)	2(2.7)	5(3.3)	0.207	0.649
No	72(96.0)	73(97.3)	145(96.7)		
Drink alcohol					
Yes	10(13.3)	7(9.3)	17(11.3)	0.597	0.440
No	65(86.7)	68(90.7)	133(88.7)		
Hypertension					
Yes	21(28.0)	3(4.0)	24(16.0)	16.071	0.000
No	54(72.0)	72(96.0)	126(84.0)		

Serum malondialdehyde level in women with high-risk human papilloma virus

MDA (nmol/L)					
HPVDNA	N	Mean	Std. Deviation	Minimum	Maximum
Positive	75	5.96913	2.992795	1.438	11.044

Serum malondialdehyde level in women without high-risk human papilloma virus infection

MDA (nmol/L)					
HPVDNA	N	Mean	Std. Deviation	Minimum	Maximum
Negative	75	0.34036	0.225598	0.065	0.980

	HPV	N	Mean	Std. Deviation	t-test	Pvalue
MDA (nmol/L)	HPV Negative	75	.34036	.225598	16.242	<0.001
	HPV Positive	75	5.96913	2.992795		

DISCUSSION

The findings of this study underscore the significant differences in serum malondialdehyde (MDA) levels between HPV-negative and HPV-positive women, particularly in the context of HIV infection in a tertiary hospital in Nigeria. Serum MDA, a biomarker of lipid peroxidation and oxidative stress, was markedly elevated in HPV-positive women compared to their HPV-negative counterparts. This result aligns with previous studies indicating that HPV infection is associated with oxidative stress, a known driver of carcinogenesis.

The study revealed a statistically significant difference in serum MDA levels, with HPV-positive women exhibiting mean levels of 5.97 ± 2.99 nmol/L compared to 0.34 ± 0.23 nmol/L in HPV-negative women ('p' < 0.001). This stark contrast underscores the oxidative stress induced by HPV infection, which may exacerbate the progression of cellular damage and increase susceptibility to cervical intraepithelial neoplasia and, potentially, cervical cancer. The elevated oxidative stress observed in HPV-positive women may be attributed to HPV's ability to disrupt cellular antioxidant defenses through the actions of viral oncoproteins E6 and E7, which impair tumor suppressor pathways and promote the production of reactive oxygen species (ROS). In comparison, a study conducted in South Africa by Xulu et al.[1] also demonstrated elevated MDA levels in HPV-positive women, particularly among HIV-positive individuals. Their findings emphasized the synergistic effect of HIV on HPV-related oxidative stress, mirroring this study's outcomes. Similarly, a study in Kenya by Othieno-Abinya et al.[17] found higher oxidative stress markers among HPV-positive women, reinforcing the role of lipid peroxidation in HPV pathogenesis.

Globally, studies from regions such as Asia and Europe corroborate these findings. For instance, research in India by Patel et al.[18] highlighted elevated MDA levels in HPV-positive women, linking these changes to oxidative stress-induced cervical epithelial damage. Similarly, a European cohort study by Martin-Hirsch et al.[18] demonstrated increased oxidative stress biomarkers in HPV-infected women, regardless of HIV status, further validating the association between HPV and lipid peroxidation. These studies underscore the universality of oxidative stress as a critical factor in HPV-related pathology while highlighting regional nuances in socio-demographic and clinical variables.

Socio-demographic factors played a significant role in HPV infection patterns. Age emerged as a significant factor, with the majority of HPV-positive women falling within the 31–40 and 41–50 age groups ('p' = 0.011). These findings are consistent with the epidemiology of HPV infection, which often peaks in sexually active women within these age ranges. Education level was also significantly associated with HPV status, with tertiary education being more prevalent among HPV-positive women ('p' < 0.001). This may reflect better health-seeking behavior and access to screening services in more educated populations, leading to higher detection rates.A Tanzanian study by Kapinga et al. (2019) also identified age and education level as key socio-demographic determinants of HPV infection, particularly among women attending HIV clinics. This study's findings align with the broader African context, where disparities in education and health literacy influence HPV awareness and detection.

Awareness of contraception was significantly higher among HPV-positive women ('p' = 0.007), although a history of contraceptive use did not show a statistically significant association ('p' = 0.161). This suggests that while awareness may influence health-seeking behavior, other factors, such as the type and duration of contraceptive use, might play a more nuanced role in modulating HPV infection risk. Interestingly, lifestyle factors such as smoking and alcohol consumption were not significantly associated with HPV status, which may reflect cultural or regional differences in these behaviors among the study population. Similar findings were reported in a Ugandan study by Tumwesigye et al.[1] which found that contraceptive awareness was higher among HPV-positive women but noted no significant relationship with contraceptive use. The authors attributed this to variations in hormonal contraceptive types and their potential impact on cervical epithelial changes.

The elevated serum MDA levels in HPV-positive women, particularly in the context of HIV infection, highlight the compounded oxidative stress in this population. HIV infection is known to impair immune surveillance, allowing HPV to persist and exacerbate oxidative damage. This dual burden of infections may accelerate cervical dysplasia progression and underscores the need for targeted interventions, including antioxidant therapies, in HPV-positive, HIV-infected women.

CONCLUSION

In conclusion, this study demonstrates a significant elevation in serum MDA levels among HPV-positive women, highlighting the role of oxidative stress in HPV-related pathophysiology. The findings underscore the need for integrated approaches that combine HPV prevention, early detection, and management strategies with interventions targeting oxidative stress, particularly in high-risk populations such as HIV-infected women. Addressing the socio-demographic determinants of HPV infection will be critical in reducing the burden of cervical cancer in Nigeria.

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