World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

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Myeloperoxidase Activities Under Highly Effective Host Immunological Control of HIV-1 Disease Progression

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World Journal of Advanced Research and Reviews, 2025, 28(01), 093-104

Publication history: Received on 17 August 2025; revised on 25 September 2025; accepted on 30 September 2025

Article DOI: https://doi.org/10.30574/wjarr.2025.28.1.3337

Abstract

Myeloperoxidase (MPO), a neutrophil-derived enzyme, plays a critical role in oxidative host defense and inflammatory modulation during HIV infection. While untreated HIV and early antiretroviral therapy (ART) phases are associated with increased MPO activity, its behavior under highly effective immunological control remains unclear.

This cross-sectional study enrolled 40 participants: 30 HIV-1–infected individuals (10 OFF-HAART, 10 ON-HAART, 10 AIDS progressors) and 10 HIV-negative controls. Socio-demographic, immunological, and biochemical parameters were assessed, and MPO activity was measured by dianisidine-H_2O_2 assay. Correlation and ROC analyses evaluated associations with HIV progression markers.

Age and gender significantly associated with HIV stage ($p = 0.002$ and $p = 0.013$, respectively), with AIDS progressors predominantly ≤30 years (60%) and male (80%). HAART duration was also significant ($p = 0.011$), but infection duration showed no difference ($p = 0.653$). Circulating MPO activity did not differ significantly across groups ($p = 0.629$), with slightly higher levels in HIV-negative controls (0.11 ± 0.02 U) versus OFF-HAART (0.08 ± 0.02 U), ON-HAART (0.08 ± 0.02 U), and AIDS progressors (0.07 ± 0.02 U). MPO activity inversely correlated with viral load ($r = -0.413$, $p = 0.023$), CD8 count ($r = -0.335$, $p = 0.035$), and WBC ($r = -0.339$, $p = 0.032$), but not CD4 count or IL-8. CD4 strongly correlated negatively with viral load ($r = -0.562$, $p = 0.001$) and positively with albumin ($r = 0.609$, $p < 0.001$). ROC analysis showed CD4 had the highest predictive accuracy (AUC = 0.895, $p = 0.001$), while MPO showed fair discrimination (AUC = 0.653, $p = 0.180$).

Despite significant immune perturbations in HIV-positive individuals, systemic MPO activity did not increase compared to controls, possibly reflecting tissue compartmentalization or sampling limitations. However, inverse correlations with viral load suggest a potential role for MPO in immunological control, warranting longitudinal and mechanistic studies.

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Keywords: Myeloperoxidase; HIV-1; Host immunological control; Disease progression; Innate immunity; Oxidative stress; Inflammation

1. Introduction

Myeloperoxidase (MPO) is a heme-containing peroxidase enzyme primarily stored in neutrophil azurophilic granules, where it plays a key role in innate immunity by generating potent oxidants such as hypochlorous acid (HOCl) to eliminate pathogens. Beyond its antimicrobial function, MPO and its oxidative products have been implicated in promoting endothelial dysfunction, lipid peroxidation, and chronic inflammatory states, thereby contributing to cardiovascular and metabolic complications (Kargapolova et al., 2021). In the context of HIV-1 infection, persistent immune activation and oxidative stress are well-recognized drivers of disease progression and non-AIDS-related comorbidities, even in individuals on antiretroviral therapy (ART) with long-term viral suppression (Zicari et al., 2019), HIV infection, particularly in ART-naïve individuals, is associated with elevated MPO activity and increased neutrophil oxidative burst, which peak shortly after ART initiation and normalize only after prolonged viral suppression (≥2 years) (Lombardi et al., 2024). Conversely, data from virally suppressed adults including elite controllers suggest that systemic MPO levels may remain comparable to those of HIV-negative individuals, despite evidence of sustained neutrophil extracellular trap (NET) formation and subclinical inflammation (Rodrigues et al., 2023). This discrepancy highlights a critical knowledge gap regarding MPO dynamics under highly effective host immunological control of HIV-1, whether achieved naturally or through potent ART regimens. While ART and elite control reduce viral replication and restore CD4+ T-cell counts, chronic immune activation and oxidative imbalance persist in many individuals (Sarr et al., 2021), contributing to cardiovascular and metabolic complications. MPO, as a major oxidative enzyme, may influence these outcomes, yet its precise role under conditions of strong immunological control remains poorly defined. Clarifying MPO activity under highly effective host immunological control is essential for understanding residual inflammation in HIV infection, refining biomarkers for oxidative stress, and identifying potential therapeutic targets to mitigate comorbidities. Given the growing burden of non-AIDS-related complications in people living with HIV, this investigation holds significant clinical relevance.

2. Materials and method

2.1. Methodology

A total of forty participants were enrolled in this study, comprising thirty HIV-1–infected individuals receiving care at the Hope Clinic, State Specialist Hospital, Asubiaro, Osogbo, Osun State, South-Western Nigeria, and ten HIV-negative individuals who served as controls. Among the HIV-positive participants, 50% were on effective oral highly active antiretroviral therapy (HAART), consisting of Tenofovir (300 mg/day), Lamivudine (150 mg/day), and Efavirenz (600 mg/day). Pregnant women and individuals co-infected with tuberculosis and/or hepatitis viruses were excluded. HIV-positive participants who were HAART-naïve were asymptomatic and had CD4+ T-cell counts greater than 200 cells/μL at the time of enrollment. Ethical approval for the study was obtained from the Research Ethics Committee of the Osun State Hospitals Management Board, and written informed consent was secured from all participants.

2.2. Sampling, Processing and Preservation

Blood sampling was done by venepunture while using appropriate standard method. Specimen was transported under ice- cold condition to the laboratory within one hour. Serum was separated from the whole blood by centrifugation at 1,000rpm for ten minutes and stored at -70^{0}c plasma was also stored at -70^{0}c.

2.3. Determination of Myeloperoxidase Activities

MPO activity was determined by a dianisidine-H_2O_2 method (Bradley et al., 1982), modified for 96-well plates. Briefly, plasma samples (10 μg protein) were added in triplicate to 0.53 mM *o*-dianisidine dihydrochloride (Sigma) and 0.15 mM H_2O_2 in 50 mM potassium phosphate buffer (pH 6.0). After incubation for 5 min at room temperature, the reaction was stopped with 30% sodium azide, and the change in absorbance was measured at 460 nm (ε = 11,300 $M^{-1}\cdot cm^{-1}$). Results were expressed as units of MPO/mg protein, whereby 1 unit of MPO was defined as the amount of enzyme degrading 1 nmol H_2O_2 per min at 25°C.

MPO protein content was determined by ELISA (Chang et al., 2006); 96-well microtiter plates were coated overnight at 4°C with 100-μl serum samples in 0.1 M carbonate buffer, pH 9.6 (1:10 [vol/vol]), and blocked for 2 h at room temperature with 1% nonfat dry milk. Plates were then sequentially incubated with 100 μl each of anti-MPO monoclonal antibody (Abcam) (1:4,000) for 2 h, horseradish peroxidase-labeled IgG antibody (Sigma) (1:5,000) for 1 h, and Sure

Blue TMB substrate for 20 min. The colorimetric change in absorbance was measured at 650 nm on a SpectraMax 190 microplate reader (Molecular Devices). Haematology parameters were analysed in haematology auto analyser Sysmex KX-21 which analyses using three detector blocks.

2.4. Statistical Analysis

Data were analyzed using graph prism version 5 software package (San Diego, CA) to determine Spearman correlation and Fisher's test were used to test the association between two variables. Results were expressed as Mean ± Standard Error of Means (SEM). The level of statistical significance were considered $p<0.05$.

3. Result

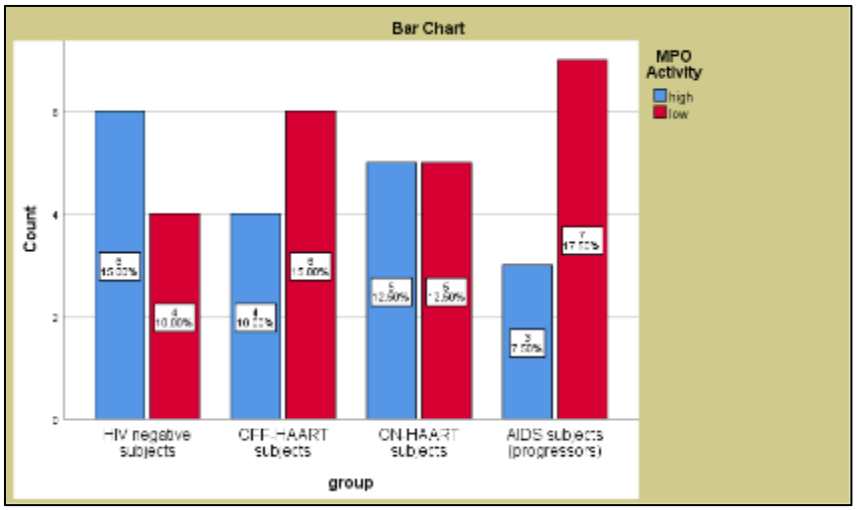
The socio-demographic analysis revealed significant associations of HIV status with age ($p = 0.002$) and gender ($p = 0.013$). Most HIV-negative and OFF-HAART participants were aged 31–50 years, whereas AIDS progressors were predominantly ≤30 years, and ON-HAART subjects were more often ≥51 years. Males constituted the majority among AIDS progressors, while females predominated in HIV-negative and OFF-HAART groups (table 1). Infection duration showed no significant difference ($p = 0.653$), although most participants had lived with HIV for 1–10 years. HAART duration varied significantly across groups ($p = 0.011$), (table 2) presents the immunological and biochemical markers among study groups. The crosstabulation between HIV status groups and MPO activity (high vs. low) revealed no statistically significant association ($\chi^2 = 2.020$, df = 3, $p = 0.568$). High MPO activity was most frequent among HIV-negative subjects (15.0%) and least common among AIDS progressors (7.5%), whereas low MPO activity was highest in AIDS progressors (17.5%) and lowest in HIV-negative participants (10.0%). ON-HAART and OFF-HAART groups showed a balanced distribution between high and low MPO activity (12.5% each for ON-HAART; 10.0% and 15.0% for OFF-HAART) (figure 2). A significant correlations was observed between myeloperoxidase (MPO) activity and several HIV-1 disease progression markers. MPO exhibited a negative correlation with CD8 count ($r = -0.335$, $p = 0.035$), viral load ($r = -0.413$, $p = 0.023$), and WBC ($r = -0.339$, $p = 0.032$), suggesting reduced MPO activity is associated with higher viral replication and altered immune cell dynamics. CD4 count was strongly negatively correlated with viral load ($r = -0.562$, $p = 0.001$) but positively correlated with albumin ($r = 0.609$, $p < 0.001$), indicating better nutritional status with higher immunity. CD8 count correlated positively with WBC ($r = 0.521$, $p = 0.001$) and interleukin-8 (IL-8) ($r = 0.427$, $p = 0.006$), reflecting immune activation. IL-8 also correlated positively with WBC ($r = 0.330$, $p = 0.037$) and neutrophils ($r = 0.346$, $p = 0.029$), emphasizing its role in inflammation (Table 3). Immunological and biochemical parameters across HIV disease stages and MPO activity groups reveals significant differences in CD4 count ($p = 0.001$), viral load ($p = 0.002$), and albumin ($p = 0.018$). CD4 counts were highest among AIDS progressors with low MPO (828.57±67.77) and lowest in OFF-HAART with high MPO (143.75±76.19), indicating severe immunosuppression in untreated patients with elevated oxidative activity. Viral load was markedly higher in OFF-HAART groups compared to ON-HAART, with low MPO individuals showing the greatest viral replication (319,436.83±116,747.96). Albumin levels were generally higher in HIV-negative and AIDS progressor groups compared to OFF-HAART and ON-HAART patients, suggesting a link between hypoalbuminemia and disease stage. Interleukin-8 levels varied widely, being extremely elevated in HIV-negative individuals with low MPO (423.58±139.88) compared to other groups, but this was not statistically significant ($p = 0.088$). Total protein and globulin showed marked variability, especially in ON-HAART (low MPO), but without significant group differences. WBC, neutrophil, and lymphocyte counts did not differ significantly across groups (Table 4).

Table 1 Socio-demographic Characteristics and HIV Status Distribution**.**

Variable	Categories	HIV-Negative n(%)	OFF-HAART n(%)	ON-HAART n(%)	AIDS (Progressors) n(%)	χ^2	df	p-value
Age (years)	≤30 years	0(0.0%)	0(0.0%)	1(10.0%)	6(60.0%)	20.783	6	0.002
	31–50 years	9(90.0%)	8(80.0%)	5(50.0%)	3(30.0%)			
	≥51 years	1(10.0%)	2(20.0%)	4(40.0%)	1(10.0%)			
Gender	Male	3(30.0%)	1(10.0%)	4(40.0%)	8(80.0%)	10.833	3	0.013
	Female	7(70.0%)	9(90.0%)	6(60.0%)	2(20.0%)			

Infection Duration (years)	1–10 years	–	6(60.0%)	5(50.0%)	11(55.0%)	0.202	1	0.653
	11–20 years	–	4(40.0%)	5(50.0%)	9(45.0%)			
HAART Duration (years)	<5 years	–	6(60.0%)	1(10.0%)	7(35.0%)	11.238	3	0.011
	6–10 years	–	0(0.0%)	4(40.0%)	4(20.0%)			
	11–15 years	–	4(40.0%)	2(20.0%)	6(30.0%)			
	16–20 years	–	0(0.0%)	3(30.0%)	3(15.0%)			

Nature of HAART: Tenofovir (300 mg/day), lamivudine (150 mg/day) and Efaviren (600 mg/day)



(χ^2 = 2.020, df = 3, p = 0.568).

Figure 1 Myeloperoxidase activities among the study group

Table 2 Immunological and Biochemical Markers among Study Groups

Parameter	HIV Negative Subjects	OFF-HAART Subjects	ON-HAART Subjects	AIDS Subjects (Progressors)	p-Value
CD4 (cells/μL)	603.80 ± 69.18	166.10 ± 41.40	395.20 ± 61.69	782.60 ± 60.41	0.000
% CD4	6.04 ± 0.69	1.66 ± 0.41	3.95 ± 0.62	7.83 ± 0.60	0.000
Viral Load (copies/mL)	4202.70 ± 716.26	299173.90 ± 72209.63	171861.80 ± 57852.45	–	0.002
WBC (cells/μL)	4480.00 ± 460.87	4460.00 ± 543.90	4290.00 ± 498.32	3920.00 ± 367.21	0.824
Neutrophil (%)	46.20 ± 5.06	50.10 ± 5.76	41.00 ± 4.32	40.30 ± 4.30	0.455
Absolute Neutrophil	2123.40 ± 353.88	2366.10 ± 433.31	1794.00 ± 303.98	1584.80 ± 232.80	0.385
Lymphocyte (%)	53.80 ± 5.06	49.90 ± 5.76	59.00 ± 4.32	59.70 ± 4.30	0.455
Interleukin-8 (pg/mL)	175.89 ± 84.58	211.14 ± 64.55	125.08 ± 39.73	11.40 ± 1.14	0.088

Myeloperoxidase U	0.11 ± 0.02	0.08 ± 0.02	0.08 ± 0.02	0.07 ± 0.02	0.629
Total Protein (g/dL)	80.59 ± 3.51	79.15 ± 3.93	167.99 ± 80.84	85.28 ± 5.83	0.349
Albumin (g/dL)	56.46 ± 1.64	49.43 ± 2.88	52.84 ± 1.62	58.59 ± 1.85	0.018
Globulin (g/dL)	24.13 ± 3.57	29.72 ± 4.28	115.15 ± 81.27	27.69 ± 4.15	0.336

Table 3 Association Between Myeloperoxidase Activity and HIV-1 Disease Progression Markers Across Immunological Control Groups

		MPO	**CD4**	**CD8**	**virallo ad**	**WBC**	**Neutrop hil**	**Lmph ocyte**	**Interl ukin8**	**Total protei n**	**Album in**	**Globul in**
MPO	r	1	0.03 4	-0.33 5*	-0.413*	-0.33 9*	-0.111	0.111	-0.272	-0.139	0.220	-0.152
	p		0.83 7	0.03 5	0.023	0.03 2	0.494	0.494	0.089	0.393	0.173	0.348
CD4	r	0.034	1	-0.04 0	-0.562**	-0.01 7	-0.194	0.194	-0.326*	-0.045	0.609**	-0.077
	p	0.837		0.80 8	0.001	0.91 9	0.230	0.230	0.040	0.782	0.000	0.638
CD8	r	-0.335*	-0.04 0	1	-0.256	0.52 1**	0.025	-0.025	.427**	-0.036	-0.289	-0.021
	p	0.035	0.80 8		0.173	0.00 1	0.879	0.879	0.006	0.827	0.071	0.898
virallo ad	r	-0.413*	-0.56 2**	-0.25 6	1	-0.00 8	0.310	-0.310	-0.112	0.261	-0.173	0.267
	p	0.023	0.00 1	0.17 3		0.96 7	0.096	0.096	0.555	0.164	0.361	0.153
WBC	r	-0.339*	-0.01 7	0.52 1**	-0.008	1	0.290	-0.290	0.330*	-0.179	-0.182	-0.168
	p	0.032	0.91 9	0.00 1	0.967		0.069	0.069	0.037	0.269	0.262	0.299
Neutr ophil	r	-0.111	-0.19 4	0.02 5	0.310	0.29 0	1	-1.000**	0.346*	0.051	-0.174	0.059
	p	0.494	0.23 0	0.87 9	0.096	0.06 9		0.000	0.029	0.757	0.282	0.718
Lmph ocyte	r	0.111	0.19 4	-0.02 5	-0.310	-0.29 0	-1.000**	1	-0.346*	-0.051	0.174	-0.059
	p	0.494	0.23 0	0.87 9	0.096	0.06 9	0.000		0.029	0.757	0.282	0.718

Interlukin8	r	-0.272	-0.326*	0.427**	-0.112	0.330*	0.346*	-0.346*	1	-0.105	-0.222	-0.094
	p	0.089	0.040	0.006	0.555	0.037	0.029	0.029		0.518	0.169	0.565
Totalprotein	r	-0.139	-0.045	-0.036	0.261	-0.179	0.051	-0.051	-0.105	1	-0.085	.998**
	p	0.393	0.782	0.827	0.164	0.269	0.757	0.757	0.518		0.603	0.000
Albumin	r	0.220	0.609**	-0.289	-0.173	-0.182	-0.174	0.174	-0.222	-0.085	1	-0.139
	p	0.173	0.000	0.071	0.361	0.262	0.282	0.282	0.169	0.603		0.391
Globulin	r	-0.152	-0.077	-0.021	0.267	-0.168	0.059	-0.059	-0.094	0.998**	-0.139	1
	p	0.348	0.638	0.898	0.153	0.299	0.718	0.718	0.565	0.000	0.391	

*. Correlation is significant at the 0.05 level (2-tailed); **. Correlation is significant at the 0.01 level (2-tailed).

The distribution of age, gender, and HAART duration across MPO categories shows no statistically significant associations ($p > 0.05$ in all cases). For age, most HIV-negative individuals with high MPO were within 31–50 years (60.0%), while OFF-HAART and ON-HAART groups also had higher representation in this age range, with minimal variation between high and low MPO. Among AIDS progressors, younger individuals (≤30 years) were more common in the low MPO group (50.0%). Gender distribution was generally skewed toward females in HIV-negative, OFF-HAART, and ON-HAART groups, while AIDS progressors were predominantly male, particularly in the low MPO category (60.0%). HAART duration showed no clear trend; however, ON-HAART participants with high MPO were slightly more represented in the 11–15 years category (30.0%), while those with low MPO were more frequent in the <5 years category (40.0%). Similarly, among AIDS progressors, low MPO individuals were more distributed across longer treatment durations (6–20 years) (Table 5).The AUC analysis indicates that CD4 count demonstrated the strongest predictive performance for HIV-1 progression (AUC = 0.895, $p = 0.001$), followed by albumin with moderate accuracy (AUC = 0.690, $p = 0.095$). Myeloperoxidase (MPO) showed fair discrimination (AUC = 0.653, $p = 0.180$), while viral load performed poorly (AUC = 0.100, $p < 0.001$, indicating inverse prediction). Other markers, including WBC, neutrophils, lymphocytes, interleukin-8, total protein, and globulin, had low AUC values (≤0.513), indicating minimal predictive value (Table 6).

Table 4 Comparison of Immunological and Biochemical Parameters across Group

Parameter	**HIV Negative (High MPO)**	**HIV Negative (Low MPO)**	**OFF-HAART (High MPO)**	**OFF-HAART (Low MPO)**	**ON-HAART (High MPO)**	**ON-HAART (Low MPO)**	**AIDS Progressors (High MPO)**	**AIDS Progressors (Low MPO)**	**P-Value**
CD4 (cells/μL)	647.00±108.46	539.00±64.48	143.75±76.19	181.00±52.05	531.00±80.96	259.40±36.77	675.33±119.89	828.57±67.77	0.001
Viral Load	4554.83±1037.35	3674.50±1001.23	268779.50±67218.16	319436.83±116747.96	69383.60±63834.00	274340.00±75732.45	-	-	0.002
WBC (cells/μL)	3583.33±244.15	5825.00±662.54	4100.00±1040.03	4700.00±652.69	4280.00±934.56	4300.00±493.96	3633.33±366.67	4042.86±511.23	0.824
Neutrophil (%)	44.00±7.19	49.50±7.54	38.75±5.59	57.67±7.64	34.80±3.83	47.20±7.09	45.00±6.08	38.29±5.66	0.455
Lymphocyte (%)	56.00±7.19	50.50±7.54	61.25±5.59	42.33±7.64	65.20±3.83	52.80±7.09	55.00±6.08	61.71±5.66	0.455
Interleukin-8 (pg/mL)	10.77±0.40	423.58±139.88	85.66±57.19	294.80±87.70	118.56±60.67	131.60±58.31	14.01±3.08	10.27±0.84	0.088
Myeloperoxidase	0.15±0.02	0.05±0.01	0.12±0.03	0.05±0.01	0.13±0.02	0.03±0.01	0.15±0.03	0.04±0.01	0.629
Total Protein (g/L)	83.24±3.55	76.62±7.21	85.91±6.12	74.64±4.60	92.14±2.50	243.85±162.87	98.44±1.42	79.65±7.42	0.349
Albumin (g/L)	57.11±2.63	55.48±1.50	51.15±2.77	48.29±4.60	56.60±0.76	49.08±2.03	59.41±2.33	58.24±2.55	0.018
Globulin (g/L)	26.13±4.21	21.14±6.80	34.76±5.89	26.36±5.94	35.53±2.46	194.77±162.93	39.03±0.91	22.84±4.86	0.336

Table 5 Distribution of Age, Gender, and HAART Duration by MPO Category

Variable	Categories	High MPO	Low MPO	Total	Chi-square (χ^2)	P-value
Age (HIV Negative)	31–50 years	6 (60.0%)	3 (30.0%)	9 (90.0%)	1.667	0.197
	51 and above	0 (0.0%)	1 (10.0%)	1 (10.0%)		
Age (OFF-HAART)	31–50 years	3 (30.0%)	5 (50.0%)	8 (80.0%)	0.104	0.747
	51 and above	1 (10.0%)	1 (10.0%)	2 (20.0%)		
Age (ON-HAART)	≤30 years	0 (0.0%)	1 (10.0%)	1 (10.0%)	2.200	0.333
	31–50 years	2 (20.0%)	3 (30.0%)	5 (50.0%)		
	51 and above	3 (30.0%)	1 (10.0%)	4 (40.0%)		
Age (AIDS)	≤30 years	1 (10.0%)	5 (50.0%)	6 (60.0%)	2.857	0.240
	31–50 years	1 (10.0%)	2 (20.0%)	3 (30.0%)		
	51 and above	1 (10.0%)	0 (0.0%)	1 (10.0%)		
Gender (HIV Neg)	Male	1 (10.0%)	2 (20.0%)	3 (30.0%)	1.270	0.260
	Female	5 (50.0%)	2 (20.0%)	7 (70.0%)		
Gender (OFF-HAART)	Male	0 (0.0%)	1 (10.0%)	1 (10.0%)	0.741	0.389
	Female	4 (40.0%)	5 (50.0%)	9 (90.0%)		
Gender (ON-HAART)	Male	3 (30.0%)	1 (10.0%)	4 (40.0%)	1.667	0.197
	Female	2 (20.0%)	4 (40.0%)	6 (60.0%)		
Gender (AIDS)	Male	2 (20.0%)	6 (60.0%)	8 (80.0%)	0.476	0.490
	Female	1 (10.0%)	1 (10.0%)	2 (20.0%)		
HAART Duration (ON)	< 5 years	2 (20.0%)	4 (40.0%)	6 (60.0%)	1.667	0.197
	11–15 years	3 (30.0%)	1 (10.0%)	4 (40.0%)		
HAART Duration (AIDS)	< 5 years	0 (0.0%)	1 (10.0%)	1 (10.0%)	0.873	0.832
	6–10 years	1 (10.0%)	3 (30.0%)	4 (40.0%)		
	11–15 years	1 (10.0%)	1 (10.0%)	2 (20.0%)		
	16–20 years	1 (10.0%)	2 (20.0%)	3 (30.0%)		

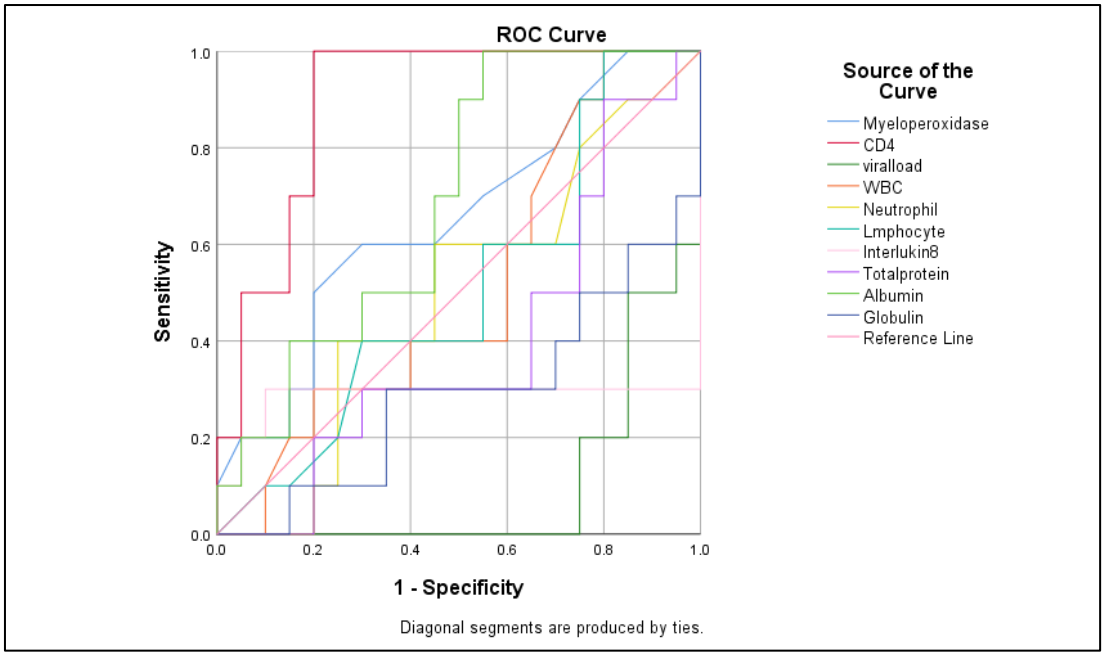


Figure 2 Receiver Operating Characteristic (ROC) Analysis of MPO and Immunological Markers

Table 6 Area Under the Curve (AUC) Analysis: Predictive Performance of MPO and Immunological Markers in HIV-1 Progression

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Myeloperoxidase	0.653	0.108	0.180	0.441	0.864
CD4	0.895	0.058	0.001	0.782	10.000
viralload	0.100	0.055	0.000	0.000	0.208
WBC	0.513	0.110	0.912	0.296	0.729
Neutrophil	0.495	0.111	0.965	0.276	0.714
Lmphocyte	0.505	0.111	0.965	0.286	0.724
Interlukin8	0.285	0.138	0.059	0.014	0.556
Totalprotein	0.395	0.110	0.356	0.180	0.610
Albumin	0.690	0.097	0.095	0.500	0.880
Globulin	0.290	0.107	0.065	0.079	0.501

4. Discussion

The socio-demographic table reveals that age and gender significantly associate with HIV disease stage: individuals aged ≤30 years are disproportionately represented among AIDS progressors (60 %), with none in negative or off-HAART groups (χ^2 = 20.783, df = 6, p = .002), while those aged 31–50 years are more prevalent among HIV-negative (90 %) and OFF-HAART (80 %) groups; gender likewise shows males more common among AIDS progressors (80 %) compared to females (20 %; χ^2 = 10.833, df = 3, p = .013). These demographic distributions may reflect underlying immunological differences influencing host control. Notably, myeloperoxidase (MPO) activity, a key marker of neutrophil activation, has been implicated in HIV progression: Rehman et al. (2023) observed elevated MPO activity and neutrophil oxidative burst in untreated HIV and early ART, normalizing after ≥2 years of therapy, suggesting heightened innate immune activation during disease advancement (Rehman et al., 2023). Moreover, studies indicate that HIV-1 can be captured

and neutralized via neutrophil extracellular traps involving MPO, indicating its role in host defense (Saitoh et al., 2012). These findings complement the demographic data: younger individuals and males, who are overrepresented among progressors, may experience stronger innate activation reflected in MPO dynamics. In contrast, the table shows no significant difference in infection duration ($p = .653$), suggesting that these innate immune signatures may operate independently of infection length. The HAART duration demonstrates significance ($\chi^2 = 11.238$, $df = 3$, $p = .011$), aligning with findings that prolonged therapy modulates MPO activity.

The immuno-biochemical profile in the table indicates that, despite the expected immune perturbation in HIV infection (markedly lower CD4 in OFF-HAART; $p < .001$) and very high viral loads in untreated subjects, circulating myeloperoxidase (MPO) activity was not elevated in infected groups in fact mean MPO (U) was slightly higher in HIV-negative participants (0.11 U) than in OFF-HAART (0.08 U), ON-HAART (0.08 U) or AIDS progressors (0.07 U) with no statistical difference ($p = .629$). This pattern contrasts with many mechanistic and clinical reports that link untreated HIV to neutrophil activation, increased MPO release and oxidative stress, and a transient rise in MPO/oxidative burst early after ART initiation that later normalizes with prolonged therapy (Rehman et al., 2023). Several non-exclusive explanations reconcile the present data with the literature, compartmentalization MPO may be sequestered in tissues or the gut lumen (so plasma measures underestimate total neutrophil degranulation) especially where microbial translocation and mucosal damage occur in HIV (Tincati et al., 2023)assay/units and timing — cross-sectional sampling can miss transient MPO spikes that occur shortly after ART start, and different MPO assays (activity versus antigen) give divergent results (Lin et al., 2024) disease stage and immune exhaustion advanced/chronically activated neutrophils may have depleted granule stores or undergo necrosis, lowering measurable circulating MPO despite ongoing oxidative injury (Madzime et al., 2021). The significant albumin differences ($p = .018$) and discordant IL-8 trends further suggest that systemic inflammatory wiring differs across groups and that MPO alone is an insufficient marker of neutrophil-driven oxidative pathology in HIV; multimarker panels and longitudinal sampling (pre- and post-ART initiation) better capture MPO dynamics as shown in recent studies (Patel et al., 2022).

The correlation analysis reveals that myeloperoxidase (MPO) activity demonstrated an inverse relationship with CD8 count, viral load, and white blood cell count, while no significant association was observed with CD4 levels, interleukin-8, or protein markers. The negative association between MPO and viral load suggests that increased MPO activity may be linked to improved immunological control and reduced HIV replication, consistent with findings that neutrophil activation and oxidative mechanisms contribute to early viral containment (Lin et al., 2024). Similarly, the inverse correlation with CD8 and white blood cell count aligns with evidence that chronic HIV infection induces neutrophil dysfunction and degranulation abnormalities, leading to diminished MPO release despite systemic inflammation (Tincati et al., 2023). Conversely, CD4 count exhibited a strong positive correlation with albumin and an inverse association with viral load, reaffirming its central role as a marker of immune restoration under effective antiretroviral therapy (Madzime et al., 2021). Interleukin-8 showed a positive relationship with CD8 and white blood cell count, reflecting its role in neutrophil-mediated chemotaxis and immune activation during uncontrolled viremia (Rehman et al., 2023). Interestingly, MPO did not correlate significantly with interleukin-8 or neutrophil count, suggesting that plasma MPO levels may not fully reflect tissue-specific neutrophil activity, supporting evidence of compartmentalized MPO release in the gut mucosa during HIV infection (Patel et al., 2022). Collectively, these findings indicate that MPO could serve as a supplementary biomarker for monitoring immune regulation, particularly under conditions of effective host immunological control of HIV progression.

The comparison of immunological and biochemical parameters across groups stratified by high and low myeloperoxidase (MPO) activity reveals distinctive patterns. Among HIV-negative individuals, high MPO was associated with higher CD4 counts and lower interleukin-8 (IL-8) compared to those with low MPO, suggesting a link between MPO and preserved immune competence in the absence of infection. In contrast, among OFF-HAART individuals, high MPO coincided with markedly lower CD4 counts and moderately lower viral load compared to their low MPO counterparts, indicating that elevated MPO in untreated HIV may reflect a compensatory neutrophil response during severe immune depletion (Rehman et al., 2023). ON-HAART individuals with high MPO exhibited substantially higher CD4 counts and lower viral load relative to those with low MPO, aligning with evidence that antiretroviral therapy restores neutrophil function and partially normalizes MPO activity (Madzime et al., 2021). Interestingly, AIDS progressors showed high MPO in a subgroup with preserved CD4 and normal albumin, while those with low MPO exhibited the highest CD4 counts, challenging the conventional assumption that MPO uniformly declines with disease progression. IL-8 levels were disproportionately higher in low MPO subgroups across several categories, consistent with studies suggesting an uncoupling between neutrophil activation and cytokine signaling during chronic immune dysregulation (Tincati et al., 2023).

The distributions of age, gender, and HAART duration across high versus low myeloperoxidase (MPO) activity categories revealed no statistically significant associations (all chi-square p-values > .05), suggesting that host

demographic or treatment duration factors do not strongly influence MPO status in varied HIV-related clinical groups. This contrasts with emerging reports demonstrating that MPO enzymatic activity is elevated in HIV-positive individuals on suppressive HAART and correlates with CD4 count dynamics, indicating a possible role of oxidative stress markers in residual immune perturbations (Amegashie et al., 2025). Moreover, in vitro studies have demonstrated direct virucidal activity of MPO against HIV-1 in infected T cells, implying a possible innate immunological mechanism capable of limiting viral persistence under certain conditions (Chochola et al., 1994). However, while the table's findings imply demographic and HAART-duration neutrality in MPO activity, the literature emphasizes that MPO experiences complex regulation under HAART and immune recovery contexts (Amegashie et al., 2025), and that MPO may exert direct antiviral effects independently of those demographic variables. Thus, although age, gender, and HAART exposure do not appear to stratify MPO levels statistically in this cohort, the broader biomedical evidence situates MPO as a potentially significant immunological effector in the control of HIV-1, warranting further focused investigation.

5. Conclusion

The study demonstrates that age and gender significantly influence HIV disease progression, with younger individuals (≤30 years) and males predominantly represented among AIDS progressors, while those aged 31–50 years were more common in HIV-negative and OFF-HAART groups. HAART duration was also significant, highlighting its role in immunological outcomes. Immuno-biochemical analysis revealed no significant elevation of circulating MPO activity in HIV-positive individuals compared to HIV-negative controls, despite literature linking untreated HIV and early ART initiation to increased MPO and oxidative stress. Instead, MPO levels were slightly higher in HIV-negative participants, suggesting possible compartmentalization, timing of sampling, or assay variability. Correlation analysis indicated MPO inversely related to viral load and CD8 count, aligning with its potential role in early viral control, though no association was found with CD4 or IL-8.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest

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