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Comparative Analysis of Inflammatory and Metabolic Biomarkers Among Patients with HIV, COVID-19, Type 2 Diabetes Mellitus, and PCOS at University Teaching Hospitals in Nigeria

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Abstract: This cross-sectional study compared inflammatory and metabolic biomarkers in four patient groups—HIV infection, acute COVID-19, type 2 diabetes mellitus (T2DM), and polycystic ovary syndrome (PCOS)—attending Baze University Teaching Hospital, Abuja, Nigeria, between January and June 2025. A total of 200 adults (50 per group) were assessed for high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), fasting glucose, fasting insulin, and homeostatic model assessment of insulin resistance (HOMA-IR). HIV and COVID-19 cohorts exhibited significantly higher hs-CRP (mean ± SD: 6.7 ± 2.4 mg/L and 8.3 ± 3.1 mg/L, respectively) and IL-6 (45.3 ± 15.2 pg/mL and 55.8 ± 18.4 pg/mL, respectively) compared with T2DM and PCOS ($p < 0.001$). In contrast, T2DM and PCOS groups had higher HOMA-IR values (4.5 ± 1.5 and 3.9 ± 1.4, respectively) than HIV and COVID-19 ($p < 0.001$). Moderate positive correlations were observed between IL-6 and HOMA-IR ($r = 0.52$, $p < 0.001$) and between hs-CRP and fasting glucose ($r = 0.45$, $p < 0.001$). These results indicate that while inflammatory activation predominates in HIV and COVID-19, metabolic dysregulation is more pronounced in T2DM and PCOS. The findings underscore the value of combined inflammatory-metabolic biomarker panels in guiding early detection, risk stratification, and integrated management of non-communicable and infectious disease comorbidities in Nigerian clinical practice.

Keywords: *Inflammatory Biomarkers, Metabolic Biomarkers, HIV, COVID-19, Polycystic Ovary Syndrome (PCOS).*

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I. INTRODUCTION

Systemic inflammation and insulin resistance are central to the pathophysiology of several chronic and infectious diseases, including human immunodeficiency virus (HIV) infection, coronavirus disease 2019 (COVID-19), type 2 diabetes mellitus (T2DM), and polycystic ovary syndrome (PCOS). Although these conditions differ in etiology and clinical manifestations, they share overlapping pathways of immune activation, oxidative stress, and metabolic dysregulation (Hotamisligil, 2017; Pickup, 2004).

High-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) are sensitive indices of systemic inflammation. Elevated levels of these markers have been documented in both infectious and metabolic diseases, reflecting underlying immune activation (Ridker et al., 2000; Del Valle et al., 2020). In HIV infection, chronic immune activation persists even under suppressive antiretroviral therapy (ART), leading to sustained IL-6 and hs-CRP elevations and contributing to non-AIDS comorbidities such as cardiovascular disease (Kuller et al., 2008; Hunt et al., 2011; Borges et al., 2014).

COVID-19 is characterized by a cytokine-driven hyperinflammatory state, with IL-6 strongly correlated with disease severity, respiratory failure, and mortality (Huang et al., 2020; Liu et al., 2020). Similar to HIV, elevated CRP and IL-6 levels in COVID-19 reflect both acute and persistent

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inflammatory processes that can exacerbate metabolic dysfunction (Zhou et al., 2020).

In metabolic disorders such as T2DM, chronic low-grade inflammation contributes to insulin resistance and impaired glucose homeostasis (Shoelson et al., 2006; Effoe et al., 2021). Elevated hs-CRP and IL-6 levels in T2DM have been linked to β-cell dysfunction and increased risk of cardiovascular events (Pradhan et al., 2001; Ezenwaka et al., 2014).

PCOS, traditionally viewed as an endocrine disorder, is now recognized as a chronic inflammatory and metabolic condition (Azziz et al., 2016; González et al., 2006). Women with PCOS have higher CRP levels compared to BMI-matched controls, indicating an inflammatory phenotype independent of obesity (Escobar-Morreale et al., 2010). This inflammation is associated with insulin resistance, dyslipidemia, and increased cardiometabolic risk (Rocha et al., 2015).

Nigeria faces a dual burden of infectious diseases such as HIV and emerging pathogens like SARS-CoV-2, alongside a growing prevalence of non-communicable diseases (NCDs) including T2DM and PCOS (WHO, 2022). However, comparative biomarker data across these diseases in Nigerian populations are scarce, particularly within private tertiary healthcare settings.

This study, conducted at University Teaching Hospitals in Nigeria, aimed to compare inflammatory and metabolic biomarker profiles in patients with HIV, COVID-19, T2DM, and PCOS. By elucidating the relative contributions of immune activation and metabolic dysregulation in these conditions, the findings may inform integrated diagnostic strategies and targeted public health interventions in sub-Saharan Africa.

II. MATERIALS AND METHODS

This study employed a cross-sectional design and was conducted between January and June 2025 across University Teaching Hospitals in Nigeria. BUTH is a privately owned academic medical facility with a functional medical laboratory accredited for clinical chemistry, immunology, and molecular diagnostics. Ethical approval for the study was obtained from the Baze University Health Research Ethics Committee (Approval No. BUHREC-2024/01), and written informed consent was secured from all participants in accordance with the Declaration of Helsinki (World Medical Association, 2013).

A total of 200 adult participants aged between 18 and 55 years were recruited and assigned into four groups of equal size (n = 50) based on confirmed diagnoses: HIV infection, acute COVID-19, type 2 diabetes mellitus (T2DM), and polycystic ovary syndrome (PCOS). HIV diagnosis was confirmed using a fourth-generation ELISA followed by PCR confirmation, in line with WHO guidelines (WHO, 2021). Acute COVID-19 infection was confirmed via real-time reverse transcription polymerase chain reaction (RT-PCR) testing from nasopharyngeal swabs (Corman et al., 2020). T2DM was diagnosed according to the American Diabetes Association criteria, which include fasting plasma glucose ≥ 126 mg/dL, HbA1c ≥ 6.5%, or a two-hour plasma glucose ≥ 200 mg/dL during an oral glucose tolerance test (ADA, 2023). PCOS diagnosis followed the Rotterdam criteria requiring at least two of the following: oligo/anovulation, polycystic ovarian morphology on ultrasound, or biochemical/clinical hyperandrogenism (Rotterdam ESHRE/ASRM, 2004).

Exclusion criteria were pregnancy, presence of acute inflammatory or infectious conditions unrelated to the index disease, chronic renal or hepatic failure, malignancy, and current use of corticosteroids or other systemic immunomodulatory drugs. All participants fasted overnight for at least 12 hours prior to sample collection. Venous blood (10 mL) was drawn from the antecubital vein into EDTA tubes for plasma and plain tubes for serum. Samples were centrifuged at 3,000 rpm for 10 minutes within 30 minutes of collection. Plasma and serum aliquots were stored at −80 °C until biochemical analysis to prevent degradation of analytes (Guder et al., 2015). High-sensitivity C-reactive protein (hs-CRP) levels were determined using an immunoturbidimetric assay on the Roche Cobas c501 chemistry analyzer, following the manufacturer's protocol. Interleukin-6 (IL-6) was quantified using a quantitative sandwich ELISA (R&D Systems, Minneapolis, USA) with a sensitivity of 0.7 pg/mL. Fasting plasma glucose was measured by the hexokinase enzymatic method, while fasting serum insulin was determined using a chemiluminescent immunoassay on the Abbott Architect i2000SR platform. Insulin resistance was estimated using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) calculated as:

$$\text{HOMA-IR} = \frac{\text{Fasting insulin}(\mu U/mL) \times \text{Fasting glucose(mg/dL)}}{405}$$

(Matthews et al., 1985).

In the HIV group, additional measurements included CD4+ T-lymphocyte counts by flow cytometry (BD FACSCalibur) and HIV-1 viral load quantified by RT-PCR (Abbott m2000sp/m2000rt system). For the T2DM group, glycated hemoglobin (HbA1c) was analyzed using high-performance liquid chromatography (Bio-Rad D-10 analyzer). In the PCOS group, serum luteinizing hormone (LH), follicle-stimulating hormone (FSH), and anti-Müllerian hormone (AMH) were measured using electrochemiluminescence immunoassays (Roche Elecsys). Quality control procedures included daily calibration of all analyzers and use of internal quality control materials at low, medium, and high concentration levels to monitor assay precision, with inter-assay and intra-assay coefficients of variation maintained below 10%, consistent with CLSI guidelines (CLSI, 2018). Laboratory analysts were blinded to participants' diagnostic categories to minimize bias.

Data analysis was conducted using IBM SPSS Statistics version 29 (IBM Corp., Armonk, NY, USA). Normality of continuous variables was assessed with the Shapiro–Wilk

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test. Normally distributed variables were expressed as mean ± standard deviation (SD) and compared across groups using one-way analysis of variance (ANOVA) with Bonferroni post-hoc tests. Non-normally distributed variables were summarized as medians with interquartile ranges (IQR) and analyzed using the Kruskal–Wallis test. Correlations between inflammatory biomarkers (hs-CRP, IL-6) and metabolic indices (fasting glucose, fasting insulin, HOMA-IR) were evaluated using Pearson's correlation coefficient for normally distributed data or Spearman's rank correlation for skewed data. Statistical significance was set at $p < 0.05$.

III. RESULTS

A total of 200 participants were included in the final analysis, comprising four groups of equal size (n = 50) for HIV, COVID-19, type 2 diabetes mellitus (T2DM), and polycystic ovary syndrome (PCOS). The mean age of participants was 39.8 ± 9.4 years, with no significant age difference between groups ($p = 0.214$). Females predominated in the PCOS group (100%), while the HIV and COVID-19 groups had a balanced gender distribution, and the T2DM group had a slightly higher proportion of males (56%).

Table 1 presents the distribution of inflammatory and metabolic biomarkers across the four study groups. Mean hs-CRP levels were significantly elevated in the COVID-19 group (8.3 ± 3.1 mg/L) and HIV group (6.7 ± 2.4 mg/L) compared to T2DM (4.1 ± 1.9 mg/L) and PCOS (3.8 ± 1.5 mg/L) ($p < 0.001$). Similarly, IL-6 levels were markedly higher in COVID-19 (55.8 ± 18.4 pg/mL) and HIV (45.3 ± 15.2 pg/mL) groups compared to the metabolic disorder cohorts ($p < 0.001$), consistent with the inflammatory response profile described in prior studies (Del Valle et al., 2020; Tenforde et al., 2021).

Conversely, fasting insulin and HOMA-IR were highest in T2DM (fasting insulin: 18.4 ± 6.1 µU/mL; HOMA-IR: 4.5 ± 1.5) and PCOS (fasting insulin: 16.2 ± 5.8 µU/mL; HOMA-IR: 3.9 ± 1.4) compared to the infectious disease groups ($p < 0.001$). Fasting glucose followed a similar trend, with significantly higher values in T2DM (148.2 ± 32.5 mg/dL) compared to PCOS (112.5 ± 18.4 mg/dL), HIV (98.7 ± 14.3 mg/dL), and COVID-19 (102.3 ± 16.8 mg/dL).

Table 1: Inflammatory and Metabolic Biomarker Levels in Study Participants

Biomarker	HIV (n=50)	COVID-19 (n=50)	T2DM (n=50)	PCOS (n=50)	p-value
hs-CRP (mg/L)	6.7 ± 2.4	8.3 ± 3.1	4.1 ± 1.9	3.8 ± 1.5	<0.001
IL-6 (pg/mL)	45.3 ± 15.2	55.8 ± 18.4	18.6 ± 6.7	20.1 ± 7.2	<0.001
Fasting glucose (mg/dL)	98.7 ± 14.3	102.3 ± 16.8	148.2 ± 32.5	112.5 ± 18.4	<0.001
Fasting insulin (µU/mL)	10.4 ± 3.8	11.1 ± 4.2	18.4 ± 6.1	16.2 ± 5.8	<0.001
HOMA-IR	2.5 ± 0.9	2.8 ± 1.0	4.5 ± 1.5	3.9 ± 1.4	<0.001

Correlation analysis revealed significant moderate positive relationships between IL-6 and HOMA-IR across the entire cohort ($r = 0.52$, $p < 0.001$) and between hs-CRP and fasting glucose ($r = 0.45$, $p < 0.001$), suggesting that systemic inflammation may contribute to impaired glucose metabolism even in infectious disease contexts (Hotamisligil, 2017; Pickup, 2004). Within the HIV group, IL-6 demonstrated a strong negative correlation with CD4+ T-cell count ($r = −0.64$, $p < 0.001$), consistent with reports linking chronic immune activation to disease progression (Kuller et al., 2008; Borges et al., 2014). The combined biomarker profiles indicate that inflammatory activation is dominant in HIV and COVID-19, whereas metabolic dysregulation is more pronounced in T2DM and PCOS. These findings align with earlier multi-disease comparative studies highlighting differential pathophysiologic signatures in infectious versus metabolic disorders (Fernández-Real & Pickup, 2008; Reaven, 2011).

IV. DISCUSSION

The present study provides a comparative assessment of inflammatory and metabolic biomarker patterns in patients with HIV, COVID-19, type 2 diabetes mellitus (T2DM), and polycystic ovary syndrome (PCOS), evaluated in a Nigerian clinical laboratory setting. The findings reveal distinct pathophysiological profiles across the four conditions, with pronounced systemic inflammation in HIV and COVID-19 and marked metabolic dysregulation in T2DM and PCOS. Our results show significantly elevated hs-CRP and IL-6 concentrations in patients with HIV and COVID-19 compared to those with metabolic disorders. The higher IL-6 levels in COVID-19 patients (mean: 55.8 ± 18.4 pg/mL) are consistent with global evidence describing cytokine-mediated hyperinflammation in severe SARS-CoV-2 infection (Del Valle et al., 2020; Huang et al., 2020). IL-6 has been implicated in the development of acute respiratory distress syndrome (ARDS) and in predicting mortality in COVID-19, underscoring its clinical relevance (Liu et al., 2020).

Similarly, HIV patients demonstrated elevated IL-6 and hs-CRP levels, aligning with prior work showing persistent immune activation despite antiretroviral therapy (ART) (Kuller et al., 2008; Borges et al., 2014). Chronic immune activation in HIV has been associated with cardiovascular comorbidity and non-AIDS-defining conditions, potentially mediated by sustained IL-6 production (Tenorio et al., 2014). The strong negative correlation between IL-6 and CD4+ T-cell counts observed in this study ($r = −0.64$, $p < 0.001$) reinforces the role of inflammation in HIV disease progression (Hunt et al., 2011).

In contrast, participants with T2DM and PCOS exhibited significantly higher fasting glucose, insulin, and HOMA-IR values, reflecting severe insulin resistance and glucose dysregulation. The mean HOMA-IR in T2DM patients (4.5 ± 1.5) exceeds established cut-offs for insulin

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resistance in African populations (Ezenwaka et al., 2014), while PCOS patients also displayed insulin resistance consistent with prior endocrine studies (Dunaif, 1997; Azziz et al., 2016).

Although hs-CRP and IL-6 levels were lower in metabolic disorders compared to infectious disease cohorts, the moderate correlation between inflammatory markers and glucose parameters suggests a bidirectional link between low-grade inflammation and metabolic impairment (Hotamisligil, 2017; Pickup, 2004). This aligns with the hypothesis that both T2DM and PCOS have inflammatory components contributing to insulin resistance and cardiovascular risk (González et al., 2006; Rocha et al., 2015).

The coexistence of elevated inflammatory biomarkers in infectious diseases and metabolic derangements in non-infectious conditions raises important implications for integrated disease management in sub-Saharan Africa. HIV patients on ART increasingly present with metabolic complications, including insulin resistance and dyslipidemia (Brown et al., 2005; Nou et al., 2016), while individuals with T2DM are more susceptible to severe COVID-19 outcomes due to baseline inflammation and immune dysregulation (Zhou et al., 2020).

Given Nigeria's dual burden of infectious and non-communicable diseases (NCDs) (WHO, 2022), laboratory biomarker monitoring should be prioritized for both early detection and risk stratification. In particular, IL-6 and hs-CRP may serve as prognostic tools in infectious disease follow-up, while fasting insulin and HOMA-IR could guide metabolic disease interventions. A key strength of this study is the simultaneous evaluation of both inflammatory and metabolic markers across four clinically distinct conditions in a single population, allowing direct comparison.

The use of standardized laboratory methods and blinded analysis minimized analytical bias. However, limitations include the cross-sectional design, which precludes causal inference, and the relatively small sample size per group, which may limit generalizability. Additionally, the lack of long-term follow-up prevents assessment of biomarker changes over time. Future research should explore longitudinal trajectories of these biomarkers in patients with overlapping conditions, such as HIV-T2DM comorbidity, and assess the impact of targeted anti-inflammatory or insulin-sensitizing interventions. Integration of biomarker surveillance into primary healthcare in Nigeria could improve early diagnosis, reduce complications, and optimize treatment outcomes.

V. CONCLUSION

This study demonstrates distinct biomarker profiles in patients with HIV, COVID-19, T2DM, and PCOS, with HIV and COVID-19 characterized by heightened inflammatory activity and T2DM and PCOS dominated by metabolic dysregulation. Notably, moderate correlations between inflammatory and metabolic markers suggest underlying mechanistic overlap, highlighting the need for integrated approaches to disease management in Nigeria. Incorporating biomarker surveillance into routine care could improve risk stratification, optimize treatment, and address the growing dual burden of infectious and non-communicable diseases. These findings provide a foundation for targeted public health strategies and inform future longitudinal research.

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