
The Levels of Serum C - reactive protein and Creatine Kinase-MM in Human Immunodeficiency Virus Seropositive Subjects Co-infected with *Plasmodium falciparum*

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Abstract: The present study was designed to determine the levels of C-reactive protein and creatine kinase-MM in Nigerian naïve (stage 2) HIV seropositive subjects co-infected with *Plasmodium falciparum*. A total of 204 subjects (aged between 18 and 45 years) were randomly studied. Among these were 74 naïve (stage 2) HIV seropositive subjects (confirmed by Western blot method), 70 naïve (stage 2) HIV seropositive subjects co-infected with *P. falciparum* (confirmed by Western blot and microscopic methods respectively) and 60 apparently healthy individuals (confirmed to be negative for Human immunodeficiency virus and *P. falciparum* by Western blot and microscopic methods respectively). Absolute lymphocyte counts was estimated using Sysmex® Automated Hematology Analyzer, whereas CD4⁺ cell count was estimated using Partec® Cyflow Counter. C-reactive protein and creatine kinase was estimated using enzyme-linked immunosorbent assay methods. The creatine kinase-MM and C-reactive protein concentrations were significantly higher in HIV seropositive subjects co-infected with malaria when compared with the controls subjects (P = 0.000) respectively. Whereas the absolute lymphocyte counts and CD4⁺ T cell counts were significantly lower in HIV seropositive subjects co-infected with malaria when compared with the controls subjects (P = 0.000). The increased expression of C- reactive protein and creatine kinase-MM coupled with the decrease in absolute lymphocyte and CD4⁺ cell counts significantly contributes to the pathogenesis of HIV and *P. falciparum* infections.

Keywords: C - reactive Protein, Creatine Kinase-MM, Human Immunodeficiency Virus, Stage 2, *Plasmodium falciparum*

1. Introduction

The levels of C-reactive proteins and creatine kinase-MM are usually elevated in response to the proinflammatory cytokines (interleukin-1 and 6), whose expression are induced by microbial infection and skeletal muscle damage which are associated with human immunodeficiency virus and *Plasmodium falciparum* infections [1],[2]. It has also been reported that an elevated CRP and CK-MM are indicative of an increased risk for cardiovascular disease and colon cancer [3], [4], [5], [6], [7], [8]. Sklar et al [9] failed to find any predictive value of CRP for cardiovascular disease in HIV-infected individuals.

There is evidence of skeletal muscle damage with increased CK-MM concentration in *P. falciparum* infected African children [2]. Furthermore, the relationship between CRP and CK-MM concentrations in naïve HIV seropositive subjects co-infected with *P. falciparum* is still unclear. Based on the above reason, the study was designed to determine the levels of CRP and CK-MM in Nigerian naïve HIV seropositive subjects co-infected with *P. falciparum*. This will add to the existing level of information on Human immunodeficiency virus and *P. falciparum* infections which is beneficial.

2. Materials and Methods

2.1. Participants

This cross sectional study was conducted at Igbinedion University Teaching Hospital in Okada Community in Ovia North East local Government Area, Edo State, Nigeria. Ethical approval was obtained from IUTH Ethical Review Committee. Informed consent was obtained from all subjects before the commencement of the study. A total of 204 subjects (aged between 18 and 45 years) were randomly studied. Among these were 74 naïve (stage 2) HIV seropositive subjects (confirmed by Western blot method), 70 naïve (stage 2) HIV seropositive subjects co-infected with *P. falciparum* (confirmed by Western blot and microscopic methods respectively) and 60 apparently healthy individuals (confirmed to be negative for human immunodeficiency virus and *P. falciparum* by Western blot and microscopic methods respectively).

2.2. Blood Samples Analysis

Eight milliliters volume of venous blood sample were collected from the ante-cubital vein of the subjects using

standard laboratory collection technique and shared equally into ethylene diamine tetra acetic acid (EDTA) vacutainers and an anticoagulant free vacutainers, subsequently centrifuged at 750 x g for 15 minutes to obtain serum. The blood samples collected in EDTA were used for absolute lymphocyte counts using Sysmex® Automated Hematology Analyzer as previously described by Ehiaghe *et al* [10] whereas CD4⁺ cell count was estimated using Partec® Cyflow Counter (Germany) as described by PCC [11]. The blood samples collected in the anticoagulant free vacutainers were used for C-reactive protein estimation using enzyme-linked immunosorbent assay method as described by Ehiaghe *et al* [12]. Serum creatine kinase was estimated using enzyme-linked immunosorbent assay method as described by Ehiaghe *et al* [13].

2.3. Data Analysis

Student's t- test was used to compare independent variables. The probability values less than 0.05 were considered significant. The statistical analysis were done using SPSS version 20.0.

Table 1. Mean \pm SD values of creatine kinase (ng/ml), C-reactive protein (ng/ml), absolute lymphocyte count (cells/ μ l) and CD4⁺ T cell counts (cells/ μ l) of the HIV seropositive subjects with control subjects.

Parameters	Creatine kinase	C-reactive protein	Absolute lymphocyte count	CD4 ⁺ T cell counts
Subjects				
HIV (N = 74)	75 \pm 0.5	8.3 \pm 1.3	0.5 \pm 0.01	300 \pm 5.0
Controls(N = 60)	0.5 \pm 0.1	1.2 \pm 1.20	1.5 \pm 0.03	800 \pm 10
P values	<0.001*	<0.001*	<0.001*	<0.001*

Keys

* = significant

N = Number of subjects

HIV = HIV seropositive subjects

Table 2. Mean \pm SD values of creatine kinase (ng/ml), C-reactive protein (ng/ml), absolute lymphocyte count (cells/ μ l) and CD4⁺ T cell counts (cells/ μ l) of the HIV seropositive subjects co-infected with *P. falciparum* and the control subjects.

Parameters	Creatine kinase	C-reactive protein	Absolute lymphocyte count	CD4 ⁺ T cell counts
Subjects				
HIV+ MP(N = 70)	90.0 \pm 0.6	10.3 \pm 1.0	0.3 \pm 0.03	250 \pm 6.0
Controls(N = 60)	0.5 \pm 0.1	1.2 \pm 0.20	1.5 \pm 0.03	800 \pm 10
P values	<0.001*	<0.001*	<0.001*	<0.001*

Keys

* = significant

N = Number of subjects

HIV+ MP = HIV seropositive subjects co-infected with *P. falciparum*

Table 3. Mean \pm SD values of creatine kinase (ng/ml), C-reactive protein (ng/ml), absolute lymphocyte count (cells/ μ l) and CD4⁺ T cell counts (cells/ μ l) of the HIV seropositive subjects and HIV seropositive subjects co-infected with *P. falciparum*.

Parameters	Creatine kinase	C-reactive protein	Absolute lymphocyte count	CD4 ⁺ T cell counts
Subjects				
HIV (N = 74)	75 \pm 0.5	8.3 \pm 1.3	0.5 \pm 0.01	300 \pm 5.0
HIV + HIV+ MP(N = 70)	90 \pm 0.6	10.3 \pm 1.0	0.3 \pm 0.03	250 \pm 10
P values	< 0.001*	<0.001*	<0.001*	<0.001*

Keys

* = significant

N = Number of subjects

HIV = HIV seropositive subjects

HIV+ MP = HIV seropositive subjects co-infected with *P. falciparum*

3. Results

Table 1 shows mean \pm (SD) values of creatine kinase, C-reactive protein, absolute lymphocyte counts and CD4⁺T cell counts of the naïve HIV seropositive subjects and controls subjects. The creatine kinase and C-reactive protein concentrations were significantly higher in naïve HIV seropositive subjects when compared with the controls subjects (P <0.001) respectively. Whereas the absolute lymphocyte counts and CD4⁺ T cell counts were significantly lower in naïve HIV seropositive subjects when compared with the controls subjects (P <0.001) respectively.

Table 2 shows mean \pm (SD) values of creatine kinase, C-reactive protein, absolute lymphocyte counts and CD4⁺ T cell counts of the naïve HIV seropositive subjects co-infected with malaria and controls subjects. The creatine kinase and C-reactive protein concentrations were significantly higher in naïve HIV seropositive subjects co-infected with malaria when compared with the controls subjects (P <0.001) respectively. Whereas the absolute lymphocyte counts and CD4⁺ T cell counts were significantly lower in naïve HIV seropositive subjects co-infected with malaria when compared with the controls subjects (P < 0.001) respectively.

Table 3 shows mean \pm (SD) values of creatine kinase, C-reactive protein, absolute lymphocyte counts and CD4⁺ T cell counts of the naïve HIV seropositive subjects and naïve HIV seropositive subjects co-infected with malaria. The creatine kinase and C-reactive protein concentrations were significantly higher in HIV seropositive subjects co-infected with malaria when compared with the HIV seropositive subjects (P <0.001) respectively. Whereas the absolute lymphocyte counts and CD4⁺ T cell counts were significantly lower in naïve HIV seropositive subjects co-infected with malaria when compared with the naïve HIV seropositive subjects (P <0.001) respectively.

4. Discussion

The present cross-sectional study provides evidence that the liver and skeletal muscles are involved in a variety of complications associated with naïve HIV seropositive subjects with or without *P. falciparum* co-infections in adults. However, naïve HIV seropositive subjects with or without *P. falciparum* co-infections had significantly higher CRP and CK-MM when compared with controls. Furthermore, the CRP and CK-MM was significantly higher in the naïve HIV seropositive subjects with *P. falciparum* co-infections when compared with the naïve HIV seropositive subjects without *P. falciparum* co-infections. Thus, indicating that *P. falciparum* enhances the metabolic disturbances associated with HIV infection. Timothy et al [14] and Bryan et al [15] reported that liver and skeletal muscles are important site for HIV and *P. falciparum* sequestration, which could contribute to the metabolic disturbances and renal complications associated with HIV and *P. falciparum* infections. Renal failure and cardiovascular disease are common and life-threatening

complication in HIV and *P. falciparum* infections [11], [16]. It is possible that the microbial sequestration might damage muscle cells without inducing overt rhabdomyolysis (Serum CK-MM concentration > 1000U/L) which is absent in these study.

The naïve HIV seropositive subjects with or without *P. falciparum* co-infections had significantly lower absolute lymphocyte count and CD4⁺ lymphocyte count when compared with controls. Furthermore, the absolute lymphocyte count and CD4⁺ lymphocyte count was significantly lower in the naïve HIV seropositive subjects with *P. falciparum* co-infections when compared with the HIV seropositive subjects without *P. falciparum* co-infections. These results indicate that elevated CRP and CK-MM had a reciprocal relationship with absolute lymphocyte count and CD4⁺ lymphocyte count in naïve HIV seropositive subjects with or without *P. falciparum* co-infections. It has been reported that HIV-infected patients correlate with a gradual reduction in absolute lymphocyte count and CD4⁺ lymphocyte count [17], [18], enumeration of CD4⁺ lymphocyte count, therefore aid in the diagnosis of HIV/AIDS, well as in the assessment of response to highly active antiretroviral therapy (HAART) [19], [20]. Although, these results suggest that CRP and CK-MM concentration may have prognostic values, such measurement should be used in combination with CD4⁺ lymphocyte count and HIV RNA levels for monitoring HIV-infected subjects on HAART.

5. Conclusion

The increased expression of C- reactive protein and creatine kinase-MM coupled with the decrease in absolute lymphocyte and CD4⁺T cell counts significantly contributes to the pathogenesis of Human immunodeficiency virus and *P. falciparum* infections. The molecular mechanism needs further investigation.

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