Research Article ISSN 2639-9458

Microbiology & Infectious Diseases

Low Mannose-Binding Lectin Levels among Individuals Co-infected with HIV/HHV-8 in the Republic of Congo

Evrard Launay Gerald Missamou[1,2], Luc Magloire Anicet Boumba[1,2,3*], Paola Candyse Tsimba[1], Dimitri Moudiongui Mboungou Malanda[1,4], Roch Bredin Bissala Nkounkou[1,5], Gervillien Arnold Malonga[1], Feddercen Kelly Helga Mayassi[1], Juste Brunhel Kaya Gondo[1], Christ Novely Balanda Nkouanga[2], Aladin Atandi-Batchy[2], Christy Parfait Nganga2 and Ghislain Loubano-Voumbi[1,2]

[1]*Faculty of Health Sciences, Marien NGOUABI University, Brazzaville, Republic of Congo.*

[2]*National Institute of Biology and Health Surveillance, Pointe-Noire, Republic of Congo.*

[3]*Pointe-Noire Research Area, National Institute for Research in Health Sciences, Pointe-Noire, Republic of Congo.*

[4]*Pathological Anatomy and Cytology Department, Brazzaville University Hospital Center, Brazzaville, Congo.*

[5]*Laboratory Service, General Hospital of Djiri, Brazzaville, Republic of Congo.*

***Correspondence:**
Dr. Luc Magloire Anicet Boumba, Faculty of Health Sciences, Marien NGOUABI University, BP 69, Brazzaville, Republic of Congo, Virologist and Molecular Biologist, Tel: +242 056601040.

Received: 28 Feb 2026; **Accepted:** 03 Apr 2026; **Published:** 14 Apr 2026

Citation: Evrard Launay Gerald Missamou, Luc Magloire Anicet Boumba, Paola Candyse Tsimba, et al. Low Mannose-Binding Lectin Levels among Individuals Co-infected with HIV/HHV-8 in the Republic of Congo. Microbiol Infec Dis. 2026; 10(2): 1-6.

ABSTRACT

Introduction: *Mannose-Binding Lectin (MBL) is a key complement lectin protein that binds to the surface of pathogens and results in activation of the complement lectin cascade. Its deficiency compromises host defense mechanisms and predisposes humans to infectious diseases. Therefore, the purpose of this study was to evaluate MBL protein expression among individuals co-infected with HIV/HHV-8 in the Republic of Congo.*

Material and Methods: *A case-control study was conducted between September 2023 and June 2024, including 170 plasma samples divided into two groups: 53 individuals co-infected with HIV/HHV-8 and 117 infected with HIV without evidence of HHV-8, HBV, and HCV infections. MBL plasma level was analyzed by ELISA. Statistical analyses were performed by R version 4.5.1, with $p < 0.05$ considered significant.*

Results: *The median age was 50 years in cases and 47 years in controls. A majority of participants were females, with 75.47% (40/53) and 70% (83/117) in the cases and controls, respectively. The median HIV viral load was at 1.77 log10 copies/ml in cases and 1.69 log10 copies/ml in controls. Most participants were receiving the first-line antiretroviral therapy (TDF + 3TC + DTG), comprising 98.11% of cases and 94.02% of controls, while 1.89% of cases and 5.98% of controls were receiving the second-line antiretroviral therapy (AZT + 3TC + ATV/r). MBL levels were significantly lower in cases compared with controls (8.36 µg/L, IQR: 5.46-11.28 µg/L, versus 23.83 µg/L, IQR: 16.38 –36.6 µg/L) with $p < 0.001$. Then, an inverse correlation was observed between HIV viral load and MBL plasma levels.*

Conclusion: *Overall, MBL plasma levels were deficient, but significantly lower in individuals co-infected with HIV/HHV-8 compared with HIV-infected individuals without evidence of HHV-8, HBV, and HCV infections.*

Keywords
Mannose-binding lectin, Level, Co-infection HIV/HHV8 and Repuiblic of Congo.

Introduction
Human herpesvirus 8 (HHV-8), also known as Kaposi's sarcoma-associated herpesvirus (KSHV), was first identified in 1994 by Chang and Moore [1]. It is a causative agent of Kaposi's sarcoma (KS), primary effusion lymphoma (PEL), and multicentric Castleman's disease (MCD) [2-4]. HHV-8 infection is ubiquitous in African regions, and an increase in the incidence of KS has been observed due to HIV infection in Africa [5]. HIV-infected population remains at approximately 800-fold high risk of KS compared with the general population, making it the most common cancer in people living with HIV (PLWH) in Africa, persists even in individuals receiving antiretroviral therapy (ART) who have an undetectable HIV load [6-9]. HHV-8 infection is required for the development of KS, MCD, and PEL, but is insufficient to induce tumorigenesis [10,11]. Precipitating factors such as immune status, environmental, and hormonal influences are involved in the pathogenesis of these diseases [11].

The host's innate response has a crucial role in controlling HHV-8 infection [12]. The first defense of the organism against pathogens such as viruses is the innate immune response [13]. It is known that viruses cross physicochemical barriers and activate pattern-recognition molecules independently of the production of specific antibodies. These molecules facilitate the phagocytosis and lysis processes of the invading pathogens, effectively interconnecting with adaptive immunity [13]. Mannose-binding lectin (MBL) is one of the innate pattern-recognition molecules and the first component of the complement lectin pathway [14]. It captures a great variety of bacteria, fungi, viruses, and parasites via recognition of the repeated patterns of sugars, present on the surface and in the capsules of these pathogens [7,15]. Some genetic alterations of the MBL-2 gene, which affect individuals, cause low serum MBL levels, resulting in defects in opsonization [13]. The expression of MBL has been associated with increased susceptibility to viral infectious diseases [14,16,17].

In the context of HIV/HHV-8 co-infection, low MBL level may further compromise host defense mechanisms, facilitating viral persistence and contributing to the progression of HHV-8–associated disease. However, data on MBL protein expression in individuals co-infected with HIV /HHV-8 remain limited, particularly in Central Africa. Therefore, this study aimed to evaluate the expression of mannose-binding lectin protein among individuals co-infected with HIV/HHV-8 in the Republic of Congo.

Methods
Study design and population
A case-control study was conducted from September 2023 to June 2024. The study population was derived from a previously described study [8]. Participants were categorized into groups: individuals co-infected with HIV/HHV-8 and infected with HIV without evidence of HHV-8, HBV and HCV infections. Cases were defined as HIV-positive individuals whose HHV-8 infection was detected by enzyme-linked immunosorbent assay (ELISA) (anti-

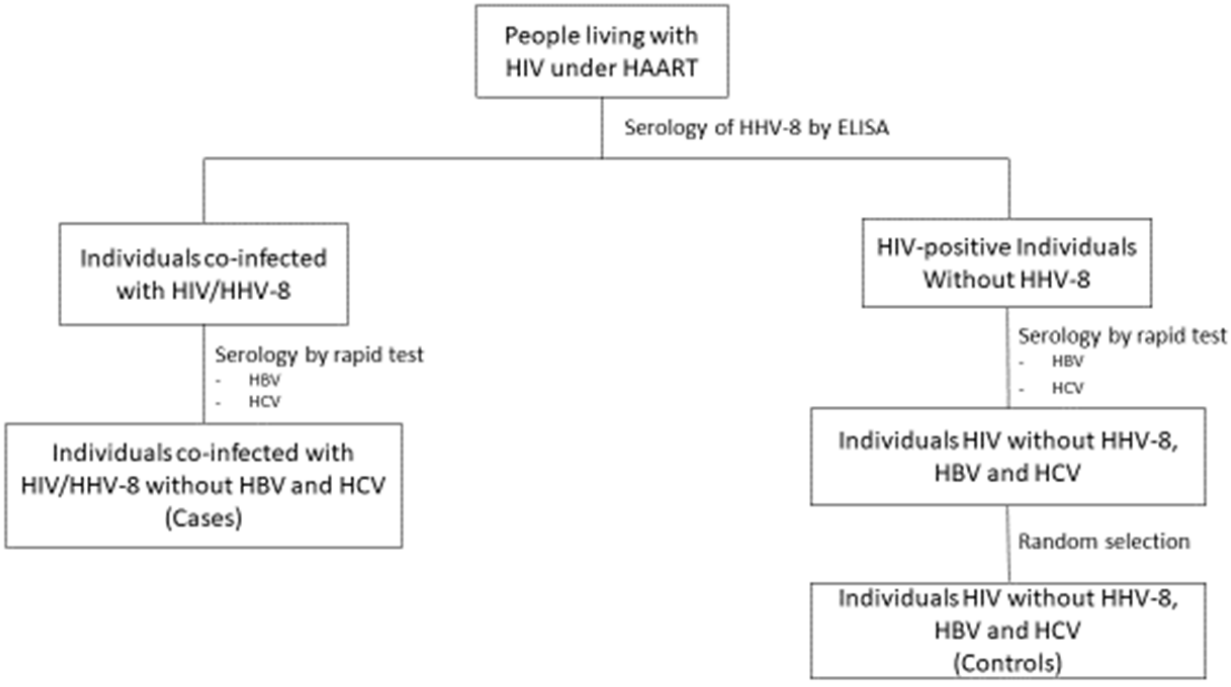

Figure 1: Flow diagram showing selected samples.

HHV-8 IgG ELISA kit, Cat No. SL2685Hu; Sunlong Biotech Co., Ltd, Hangzhou, China). Controls were defined as HIV-positive individuals who tested negative for HHV-8 infection. Inclusion criteria for cases and controls were: age ≥18 years and HIV-positive individuals under Highly Active Antiretroviral Therapy (HAART). Additional inclusion criteria for cases included confirmed HHV-8 positivity, whereas controls were required to have no evidence of HHV-8 infection. HIV-positive individuals co-infected with hepatitis B virus (HBV) and hepatitis C virus (HCV), as well as those with undetectable HIV viral load, were excluded from this study. Among them, a subset was randomly selected for the control group (Figure 1).

Data and sample collection

A structured questionnaire was administrated to all participants to collect information on sociodemographic data and HIV viral load results provided by collection sites. For each participant, whole blood samples were collected in two tubes containing ethylene diamine tetraacetic acid (EDTA). One tube was used for HIV viral load testing, which was performed on-site at the collection sites using the GeneXpert system. The second was transported to the molecular biology and virology laboratory of Marie Madeleine Gombes, where all immunological analyses were performed. Plasma was obtained after centrifugation and stored at -20°C until further analysis.

Serology of HBV and HCV

HBV and HCV infections were screened using a rapid chromatographic immunoassay (Accu-Tell® HbsAg/HCV/HIV/Syphilis Combo Test Cassette, Cat No. ABT-IDT-B78, China) according to manufacturer's instructions. This rapid test is for the qualitative detection of Hepatitis B surface antigen (HBsAg), antibodies to HCV, antibodies to HIV type 1, type 2 and syphilis antibodies (IgG and IgM) to *Treponema Pallidum* (TP) in serum or plasma. For HBsAg, the relative sensitivity was >99.9% (97.5% CI: 98.2–100%) and the relative specificity was 99.0% (95% CI: 97.2–99.8%). For anti-HCV antibodies, the sensitivity was 99.1% (95% CI: 94.9–100%) and the specificity was 99.5% (95% CI: 98.6–99.9%). For anti-HIV antibodies, the relative sensitivity of >99.99% (97.5% CI: 97.20–100%) and a relative specificity of 99.88% (95% CI: 99.57–99.99%). For syphilis, the relative sensitivity was >99.9% (95% CI: 97.7–100%) and the relative specificity was 99.7% (95% CI: 98.2–100%).

MBL plasma quantification

MBL protein levels were quantified in plasma samples using an enzyme-linked immunosorbent assay(ELISA) with a commercial ELISA kit (Human MBL Elisa kit, Cat No. SL2911Hu; Sunlong Biotech Co., Ltd, Hangzhou, China), according to the manufacturer's instructions. Briefly, 50 µL of diluted standards and plasma samples (1:5 dilution) were added to microplate wells pre-coated with an antibody specific for human MBL and incubated for 30 min at 37°C after sealing the plate. The well contents were removed, and the plates were washed five times with wash buffer. Subsequently, 50 µL of horseradish peroxidase (HRP)-conjugated reagent was added to each well, except the blank control well, and the plate was incubated for 30 min at room temperature. After washing the plate five times, 50 µL of chromogen solutions A and B were added to each well and incubated for 15 min at room temperature in the dark. The enzymatic reaction was stopped by adding 50 µL of stop solution to each well, which changed the color from blue to yellow. Absorbance was measured at 450 nm using a microplate reader (SinoThinker, Technology Co., China). MBL plasma levels were determined by reference to a standard curve generated from serial dilutions of MBL standards. The detection limit of the assay was 1 µg/L. MBL plasma level is categorized into normal (> 500 µg/L), intermediate (100 µg/L–500 µg/L) and deficient (< 100 µg/L) [18].

Statistical analysis

Data were entered into Microsoft Excel 2016 and analyzed using R version 4.5.1. Continuous variables were assessed for normality using the Shapiro-Wilk test. They were expressed as mean ± standard deviation (SD) for normal distribution, and as median with interquartile ranges (IQR) for non-normal distribution. Categorical variables were presented as frequencies with percentages. HIV viral load values were transformed to log10 copies/ml. Differences in MBL plasma levels between HIV/HHV-8 co-infected and HIV-positive individuals were assessed using the Mann–Whitney U test. Correlation between MBL plasma levels and viral load HIV was assessed using Spearman's rank correlation coefficient, with $p < 0.05$ considered significant.

Table 1: Basic characteristics of the study participants

Characteristics	Cases n=53 (%)	Controls n=117 (%)	P-value
Age (years) Median (IQR)	50 (44 -60)	47 (39 -55)	0.09
Sex			
Female	40 (75.47)	83 (70.94)	0.66
Male	13(24.53)	34 (29.06)	
Viral load HIV (log10 copies/ml) Median (IQR)	1.77 (1.6 -5.34)	1.69 (1.6 -6.62)	0.59
HIV treatment			
1st line (TDF+3TC+DTG)	52 (98.11)	110 (94.02)	0.72
2nd line (AZT +3TC+ATV/r)	1 (1.89)	7 (5.98)	1

Age and HIV viral load are represented as median (IQR).
Sex and HIV treatment are expressed as numbers and percentages

Ethical approval

The study protocol was approved by the Health Sciences Research Ethics Committee (reference number: 089/MERSIT/DGRST/CERSSA/-25), and written informed consent was obtained from each participant before enrollment.

Results

Basic characteristics of the study participants

In total, 170 samples were selected, including 53 cases with a median age of 50 years (IQR: 44-60 years) and 117 controls with a median age of 47 years (IQR: 39-55 years). A majority of participants were females, with 75.47% (40/53) and 70% (83/117) in the cases and controls, respectively. The median HIV viral load was at 1.77 log10 copies/ml (IQR: 1.6 -5.34) in cases and 1.69 log10 copies/ml (IQR: 1.6 - 6.62) in controls. Most participants were receiving the first-line antiretroviral therapy (TDF+3TC+DTG), comprising 98.11% of cases and 94.02% of controls, while 1.89% of cases and 5.98% of controls were receiving the second-line antiretroviral therapy (AZT+3TC+ATV/r) (Table 1).

Distribution of MBL plasma levels

MBL plasma levels were tested in individuals co-infected with HIV/HHV-8 and infected with HIV without evidence of HHV-8, HBV, and HCV infections (Figure 2). MBL levels were significantly lower in cases compared with controls (8.36 µg/L, IQR: 5.46-11.28 µg/L, versus 23.83 µg/L, IQR: 16.38 –36.6 µg/L, p<0.001).

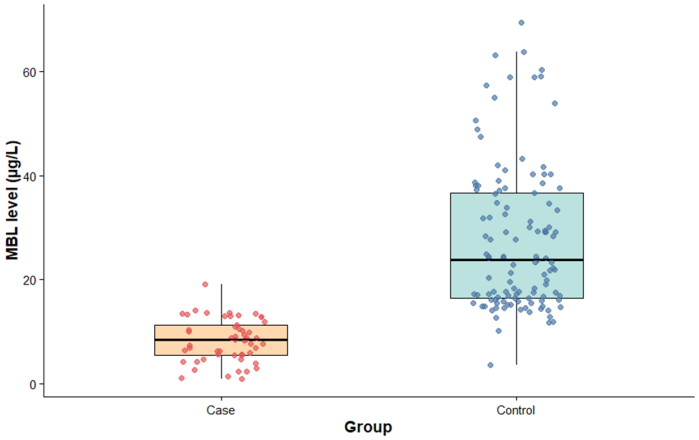

Figure 2: Distribution of MBL plasma levels among the group. Significance was assessed using the Mann–Whitney U test (p < 0.001). Bar plots represent median relative MBL plasma levels with bars indicating the range.

Correlation between MBL plasma levels and HIV viral load

We investigated the correlation between MBL plasma levels and HIV viral load. Overall, an inverse relationship was observed between HIV viral load and MBL plasma levels. In cases, the negative correlation was stronger (R = −0.24, p = 0.089), but not statistically significant, whereas in controls, a slight negative correlation was shown between HIV viral load and MBL plasma levels (R = −0.19, p = 0.041) (Figure 3).

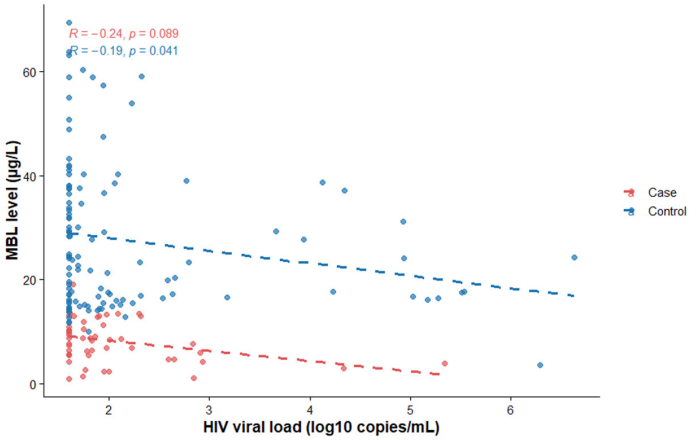

Figure 3: Correlation between MBL plasma levels and HIV viral load. The MBL plasma levels and HIV viral load correlated negatively and significantly (Spearman's rank correlation) in controls (n = 117) compared to cases (n = 53).

Discussion

The development of HHV-8-associated diseases is modulated by several factors such as host genetics, environment factors and immune status [11]. In individuals co-infected with HIV/HHV-8, HIV induces the reactivation of HHV-8 through the activation of the RTA protein [12,19]. The immune system plays a central role in controlling HHV-8 infection and limiting progression of HHV-8-associated diseases [12]. In particular, the host's innate immune response is the first line of defense against invading pathogens and is vital for the activation of the adaptive immune response [20]. In addition, MBL protein plays an important role in the innate immune response by activating the complement system during the acute phase of infection [7,21,22].

The present study is first to evaluate the expression of MBL protein among individuals co-infected with HIV/HHV-8 in the Republic of Congo. The median age was higher in cases (50 years, IQR: 44–60) than in controls (47 years, IQR: 39–55), but this difference was not statistically significant (p = 0.09). Similarly, the sex distribution did not differ significantly between groups (female: 75.5% vs 70.9%, p = 0.66). HIV viral load was also comparable between groups (median 1.77 log10 copies/mL in cases vs 1.69 log10 copies/mL in controls, p = 0.59). Most participants were receiving first-line antiretroviral therapy (TDF+3TC+DTG), with 98.1% of cases and 94.0% of controls, and no significant difference between groups (p = 0.72). This result differ with previous studies in similar populations, with a predominance of males in each group and HIV viral load detectable (median 2.752 log10 copies/mL in cases vs 2.949 log10 copies/mL in controls, p = 0.001) [7]. The observed difference might be due to sample sizes, population characteristics, and HIV treatment.

Overall, the MBL plasma levels observed in our study were deficient (< 100 µg/L) [18]. However, it was significantly lower in individuals co-infected with HIV/HHV-8 compared with HIV-infected individuals without evidence of HHV-8, HBV, and HCV infections (median 8.36 µg/L, IQR: 5.46–11.28 vs 23.83 µg/L,

IQR: 16.38–36.6; $p < 0.001$). Furthermore, an inverse correlation was observed between MBL plasma levels and HIV viral load. In cases, the negative correlation was stronger ($R = -0.24$, $p = 0.089$), whereas in controls, a weak negative correlation was observed ($R = -0.19$, $p = 0.041$). Our findings suggest a potential association between low MBL levels and HIV/HHV-8 co-infection. The lower MBL plasma levels in individuals co-infected with HIV/HHV-8 may be attributable to the consumption and reduction of this protein, involving the opsonization of HIV and HHV-8, leading to the reduction of plasma MBL levels [7]. Our results are in concordance with previous studies reporting that low MBL levels are associated with increased susceptibility to viral infections and disease progression [7,23-25]. In contrast, some studies have reported no association between MBL levels and susceptibility to viral infections [27]. MBL levels are elevated in HIV-1-infected patients and are associated with a good response to highly active antiretroviral therapy [21]. The absence of a group composed exclusively of individuals infected with HHV-8 limited our ability to assess the independent effect of HHV-8 infection on MBL protein expression, as well as the absence of $CD4^+$ T-cell count data, which restricted our capacity to comprehensively evaluate the relationship between MBL levels and immune status.

Conclusion

In conclusion, the MBL plasma levels were deficient and significantly lower in individuals co-infected with HIV/HHV-8 compared with HIV-infected individuals without evidence of HHV-8, HBV and HCV infections. Our findings support the role played by MBL in susceptibility to viral infection. They contribute to the understanding of host immune factors involved in the susceptibility of viral infection in the context of HIV infection. Further studies, we will investigate MBL gene polymorphisms and include a larger study population.

References

1. Chang Y, Cesarman E, Pessin MS, et al. Identification of herpesvirus-like DNA sequences in AIDS-sssociated kaposi's sarcoma. Science. 1994; 266: 1865-1869.
2. Lopes AO, Marinho PDN, Medeiros LDS, et al. Human Gammaherpesvirus 8 Oncogenes Associated with Kaposi's Sarcoma. Int J Mol Sci. 2022; 23: 1-15.
3. Gonçalves PH, Uldrick TS, Yarchoan R. HIV-associated Kaposi sarcoma and related diseases. AIDS. 2017; 31: 1903-1916.
4. Bower M, Carbone A. KSHV/HHV8-Associated Lymphoproliferative Disorders: Lessons Learnt from People Living with HIV. Hemato. 2021; 2: 703-712.
5. Etta EM, Alayande DP, Mavhandu-Ramarumo LG, et al. HHV-8 Seroprevalence and Genotype Distribution in Africa, 1998–2017: A Systematic Review. Viruses. 2018; 10: 1-17.
6. Malonga GA, Dienta S, Traore FT, et al. Human Herpesvirus 8 seroprevalence among blood donors in Mali. J Med Virol. 2022; 94: 4554-4558.
7. de Morais VMS, Gonçales JP, Cahú GGdOM, et al. Mannose-binding lectin concentrations in people living with HIV/AIDS infected by HHV-8. BMC immunol. 2019; 20: 1-6.
8. Missamou E, Boumba L, Bissala Nkounkou R, et al. Seroprevalence and Associated Risk Factors for Human Herpesvirus 8 Infection among People Living with HIV in Pointe-Noire and Dolisie, Republic of Congo. Advances Infec Diseases Therapy. 2025; 2: 1-6.
9. Shiels MS, Engels EA. Evolving epidemiology of HIV-associated malignancies. Curr Opin HIV AIDS. 2017; 12: 6-11.
10. Qin J, Lu C. Infection of KSHV and Interaction with HIV: The Bad Romance. Adv Exp Med Biol. 2017; 1018: 237-251.
11. Blumenthal MJ, Cornejo Castro EM, Whitby D, et al. Evidence for altered host genetic factors in KSHV infection and KSHV-related disease development. Rev Med Virol. 2021; 31: 1-13.
12. de Morais VMS, de Lima ELS, Cahú G, et al. MBL2 gene polymorphisms in HHV-8 infection in people living with HIV/AIDS. Retrovirology. 2018; 15: 1-9.
13. Barros KMA, Ribeiro Paulino M, Batista MIHdM, et al. Absence of influence of polymorphisms of the MBL2 gene in oral infections by HSV-1 in individuals with HIV. Braz J Microbiol. 2019; 50: 663-668.
14. Seppänen M, Lokki ML, Lappalainen M, et al. Mannose-binding lectin 2 gene polymorphism in recurrent herpes simplex virus 2 infection. Human immunology. 2009; 70: 218-221.
15. Neth O, Jack DL, Dodds AW, et al. Mannose-binding lectin binds to a range of clinically relevant microorganisms and promotes complement deposition. Infect Immun. 2000; 68: 688-693.
16. Boniotto M, Braida L, Pirulli D, et al. MBL2 polymorphisms are involved in HIV-1 infection in Brazilian perinatally infected children. AIDS. 2003; 17: 779-780.
17. Figueiredo GG, Cezar RD, Freire NM, et al. Mannose-binding lectin gene (MBL2) polymorphisms related to the mannose-binding lectin low levels are associated to dengue disease severity. Hum Immunol. 2016; 77: 571-575.
18. Zinyama-Gutsire RB, Chasela C, Kallestrup P, et al. HIV-1 Disease Progression and Survival in an Adult Population in Zimbabwe: Is There an Effect of the Mannose Binding Lectin Deficiency?. Omics. 2015; 19: 542-552.
19. Royston L, Jary A, Berini CA, et al. Similar Viral and Immune Characteristics of Kaposi Sarcoma in ART-treated People Living With HIV and Older Patients With Classic Kaposi Sarcoma. Open Forum Infect Dis. 2024; 11: 1-9.
20. Wang R, Lan C, Benlagha K, et al. The interaction of innate immune and adaptive immune system. Med Comm. 2024; 5: 1-37.
21. Mason CP, Tarr AW. Human lectins and their roles in viral infections. Molecules. 2015; 20: 2229-2271.
22. Martin M, Blom AM. Complement in removal of the dead - balancing inflammation. Immunological reviews. 2016; 274: 218-232.
23. Seppänen M, Lokki ML, Lappalainen M, et al. Mannose-binding lectin 2 gene polymorphism in recurrent herpes simplex virus 2 infection. Hum Immunol. 2009; 70: 218-221.

24. Szala A, Paradowska E, Nowakowska D, et al. Mannan-binding lectin-2 (MBL2) gene polymorphisms in prenatal and perinatal cytomegalovirus infections. Mol Immunol. 2011; 48: 2203-2206.

25. Garred P, Madsen HO, Balslev U, et al. Susceptibility to HIV infection and progression of AIDS in relation to variant alleles of mannose-binding lectin. Lancet. 1997; 349: 236-240.

26. Heggelund L, Mollnes TE, Ueland T, et al. Mannose-binding lectin in HIV infection: relation to disease progression and highly active antiretroviral therapy. J Acquir Immune Defic Syndr. 2003; 32: 354-361.