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Diagnostic Value of HDL-C for CD4+ T Lymphocyte Levels in ART-Naïve HIV Patients: A Retrospective Study

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Abstract

Objective and Method: Objective and Methods: To analyze the correlation between serum high-density lipoprotein (HDL-c) levels and CD4+ T lymphocyte counts in HIV patients who have not yet initiated antiretroviral therapy (ART). A retrospective study design was used to collect relevant data from newly diagnosed patients. Patients were divided into two groups based on their CD4+ T cell counts: Group A (CD4+ T cells < 200 cells/μL) and Group B (CD4+ T cells ≥ 200 cells/μL). To analyze the predictive value of HDL-C levels in diagnosing CD4+ T lymphocyte levels using SPSS software. **Results:** In the two groups of comparisons, significant differences were observed in age, CD8+ T lymphocyte count, CD4/CD8 ratio, serum uric acid level, HDL, and BLVL (lg) (BLVL). Binary logistic regression analysis after multiple iterations showed that high-density lipoprotein C and CD8+ T lymphocyte levels were positively correlated with CD4+ T lymphocyte levels, while lg (BLVL) was negatively correlated with CD4+ T lymphocyte levels. The ROC diagnostic curve results showed that when the high-density lipoprotein value was 1.015 mmol/L (AUC curve area ratio 0.596), the CD8+ T lymphocyte count was 747.5/μL (AUC curve area ratio 0.800), and the CD4/CD8 ratio was 0.283 (AUC curve area ratio 0.829). The ROC diagnostic curve results indicated that among these four factors, the CD4/CD8 ratio had the greatest diagnostic value, and the diagnostic value of high-density lipoprotein C was not inferior to that of the CD4/CD8 ratio and CD8+ T lymphocyte count. **Conclusion:** In the ROC diagnostic curve effect model, the diagnostic predictive value of HDL-c for CD4+ T lymphocytes was only higher than the baseline viral load level but inferior to the CD4/CD8 ratio and CD8+ T lymphocyte count levels. Current

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research indicates that high-density lipoprotein has limited diagnostic value as an independent predictor.

Keywords

HIV Patients, High Density Lipoprotein, CD4+T Lymphocytes, Biomarker, Diagnostic Value

1. Introduction

HIV infection remains a global public health issue. By the end of 2024, there were approximately 40.8 million people living with HIV worldwide, with 630,000 deaths from HIV-related infections and 1.3 million new infections in 2024 [1]. In 2023 (excluding Hong Kong SAR, Macau SAR, and Taiwan Region), China reported 58,903new HIV infections and 22,137 AIDS-related deaths throughout the year [2]. In 2023, Guangdong Province reported 4623 new HIV infections and 1401 deaths [3]. Metabolic indicators such as body mass index (BMI), blood lipids, uric acid, and blood glucose are commonly used as monitoring indicators for drug side effects in HIV patients. However, there are few domestic studies on the correlation between HDL levels and CD4+ T lymphocyte levels in pre-treatment HIV-infected individuals. Therefore, this article conducts further analysis based on local HIV patient data to provide clinical data support for HIV diagnosis and treatment.

2. Object and Method

2.1. Research Objectives

HIV-infected patients who visited Huizhou Sixth People's Hospital from March 2015 to December 2023 were enrolled in this study. The diagnosis of HIV infection was established based on the "Chinese AIDS Diagnosis and Treatment Guidelines (2024 Edition)" issued by the Chinese Medical Association [4]. Patients were excluded if they were transferred from other hospitals, had taken antiretroviral drugs at the time of visit, had malignant tumors, diabetes, familial hyperlipidemia, familial obesity, severe organ failure, chronic renal insufficiency, other opportunistic infections, were under 14 years old, or were pregnant or lactating HIV-infected individuals. This study was approved by the Ethics Committee of Huizhou Sixth People's Hospital (Approval No. PZ2024MI-KJ025).

2.2. Research Methods

Using retrospective research methods, we collected data from initial diagnosis patients, including age, gender, occupation, HIV infection route, educational level, height, weight, CD4+ T lymphocyte count, CD8+ T lymphocyte count, blood glucose, blood lipids, uric acid, and baseline viral load. Analyze the correlation between HDL-C and CD4+ T lymphocytes. BMI classification followed the 2024 Ministry of Health standard [5], calculated as BMI = weight/height^2 (kg/m^2). Eva-

luation criteria: <18.5 kg/m^2 for "underweight", 18.5 - 24.0 kg/m^2 for "normal weight", 24.0 - 28.0 kg/m^2 for "overweight", and ≥28.0 kg/m^2 for "obesity" [6]. According to the 2022 Chinese Guidelines for the Prevention and Treatment of Type 2 Diabetes Mellitus [7], fasting blood glucose ≥ 6.1 mmol/L or any blood glucose level ≥ 7.8 mmol/L is defined as hyperglycemia. Blood lipid management follows the 2023 Chinese Guidelines for Lipid Management [8], with hyperlipidemia defined as: total cholesterol ≥ 6.2 mmol/L, LDL ≥ 4.1 mmol/L, total triglycerides ≥ 2.3 mmol/L, non-HDL ≥ 4.9 mmol/L, and lipoprotein a ≥300 mg/L. CD4 and CD8+ T lymphocyte counts were tested by Guangzhou KingMed Diagnostics Co., Ltd., while baseline viral load was measured by Guangzhou Eighth People's Hospital.

3. Statistical Analysis

Statistical analysis was performed using SPSS 27 software: for normally distributed continuous data, analysis of variance (ANOVA) was used, expressed as mean ± standard deviation; for non-normally distributed data, rank sum test was used, expressed as M (Q1, Q3). Chi-square test was used for categorical data, expressed as percentages. Logistic regression analysis was applied to analyze the correlation between CD4+ T lymphocyte levels and other indicators. ROC curves were used to evaluate the diagnostic value of each indicator. A P-value < 0.05 was considered statistically significant.

4. Results

4.1. General

A total of 666 patients were initially enrolled, and 167 patients were excluded due to transfer from other treatment sites after receiving treatment or missing critical data such as height, weight, CD4+ T lymphocyte count, and CD8+ T lymphocyte count. Finally, 462 patients were included in the study.

Educational background: primary school accounts for 11.47%, junior high school for 41.99%, senior high school and technical secondary school for 20.56%, associate college for 14.07%, bachelor's degree for 3.46%, and others below 10% (**Figure 1**). Infection routes: Heterosexual transmission 47.62%, transmission among people have sex with same gender 39.83%, mixed sexual transmission 0.43%, and12.12% of cases did not specify transmission routes (**Figure 2**).

According to the "Chinese Guidelines for HIV/AIDS Diagnosis and Treatment (2024 Edition)", the diagnostic criteria for AIDS stage are as follows [4], patients are classified into two groups based on CD4+ T cell levels: Group A (CD4+ T cells < 200 cells/μL) and Group B (CD4+ T cells ≥ 200 cells/μL), (**Figure 3(a)**, **Figure 3(b)**). The general characteristics of both groups are as follows: Between the two groups in age ($t = 2.678$, $P < 0.01$), CD8+ T lymphocyte count ($Z = -9.844$, $P < 0.01$) (**Figure 4(a)**, **Figure 4(b)**), CD4/CD8 ratio ($Z = -10.835$, $P < 0.01$), serum uric acid level ($t = -3.160$, $P < 0.01$), high-density lipoprotein (HDL) ($t = -2.412$, $P = 0.02$), and Baseline viral load (BLVL) (lg) ($Z = -2.342$, $P = 0.02$) (**Figure 5(a)**,

Figure 5(b)) statistical comparisons revealed significant differences. However, were observed between the groups in gender distribution, same-sex transmission, fasting blood glucose (FBG), total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), or very low-density lipoprotein (VLDL) no statistically significant differences. The general situation is shown in the chart below (Table 1). And the levels of two groups of CD4+ T lymphocytes, CD8+ T lymphocytes, and BLVL are shown in the figure below (Figure 4(a), Figure 4(b), Figure 5(a), Figure 5(b)).

Table 1. General information of included cases.

	Group A (145)	Group B (317)	t/Z/x^2	P-value
Age	41.5 ± 12.88	38.11 ± 12.47	2.678	<0.01
Males or females (%)	119/26 (82.1%)	273/44 (86.1%)	1.270	0.27
BMI index number	21.41 ± 2.95	21.85 ± 3.08	−1.397	0.16
CD8+ T lymphocyte count	646 (466.25, 843.25)	1062 (788, 1403)	−9.884	<0.01
Number of people have sex with same gender intercourse (%)	50 (34.5%)	136 (42.9%)	2.932	0.09
FBG (mmol/L)	5.44 ± 1.79	5.23 ± 1.25	0.142	0.16
TC (mmol/L)	4.28 ± 1.1	4.41 ± 0.95	−1.338	0.18
TG (mmol/L)	1.25 (0.99, 1.94)	1.21 (0.86, 1.72)	−1.830	0.07
LDL (mmol/L)	2.53 (1.95, 3.10)	2.65 (2.25, 3.01)	−1.732	0.08
VLDL (mmol/L)	0.57 (0.45, 0.89)	0.55 (0.39, 0.78)	−1.827	0.07
UA (U/L)	386.93 ± 111.85	421.03 ± 105.55	−3.160	<0.01
HDL-C (mmol/L)	1.03 ± 0.33	1.10 ± 0.28	−2.412	0.02
CD4/CD8 ratio	0.16 (0.07, 0.23)	0.33 (0.22, 0.46)	−10.835	<0.01
log10 (BLVL)	4.70 (4.42, 4.88)	4.65 (4.15, 4.85)	−2.342	0.02

Abbreviation: FBG (Fasting blood glucose), TC (Total cholesterol), TG (Triglycerides), LDL (Low density lipoprotein), VLDL (Very low density lipoprotein), UA (Serum uric acid).

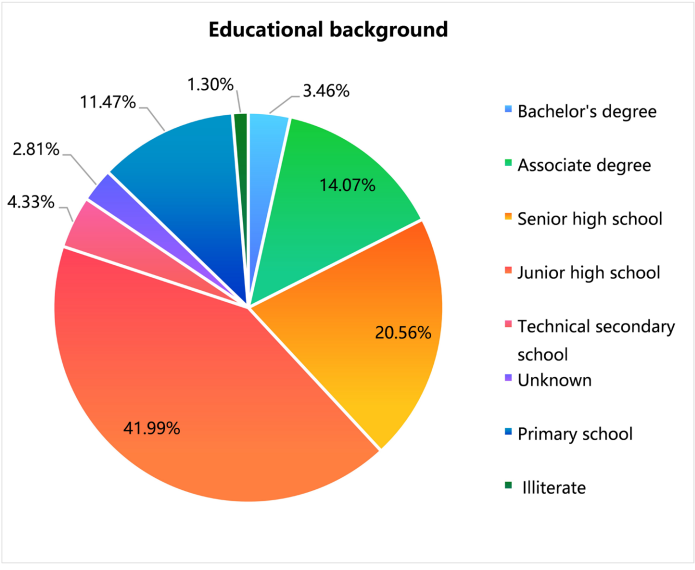


Figure 1. Education level.

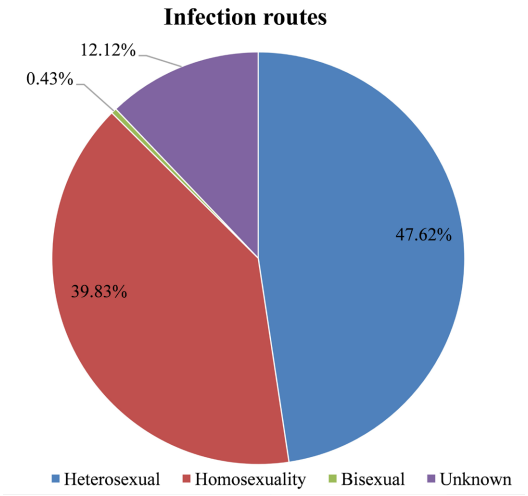
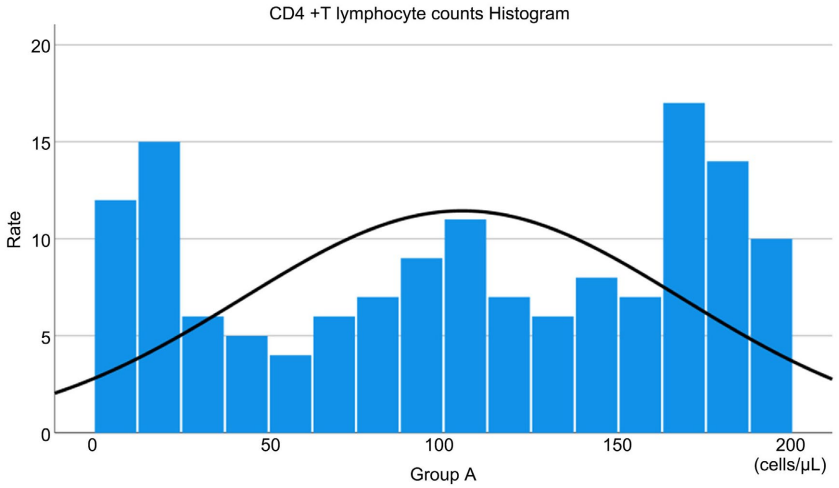
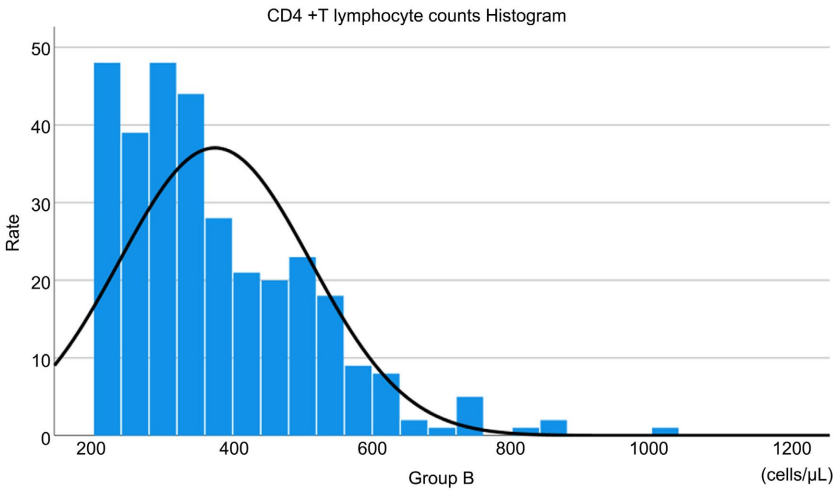


Figure 2. Proportion of infection routes.

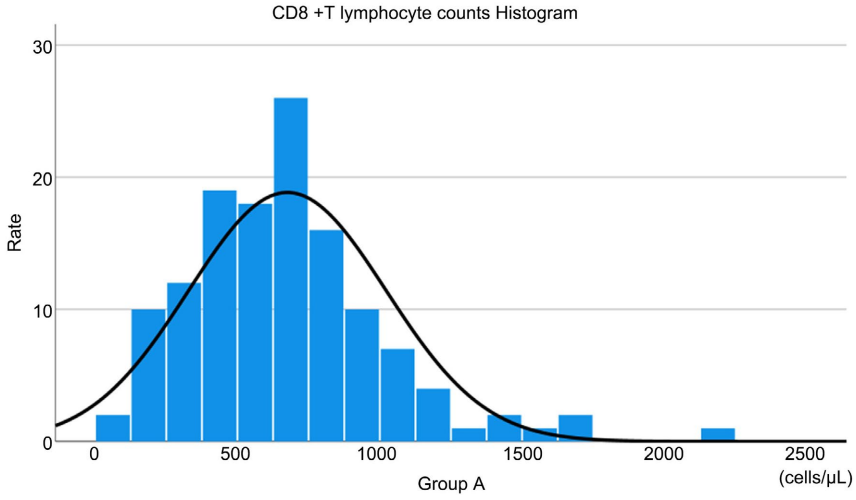


(a)

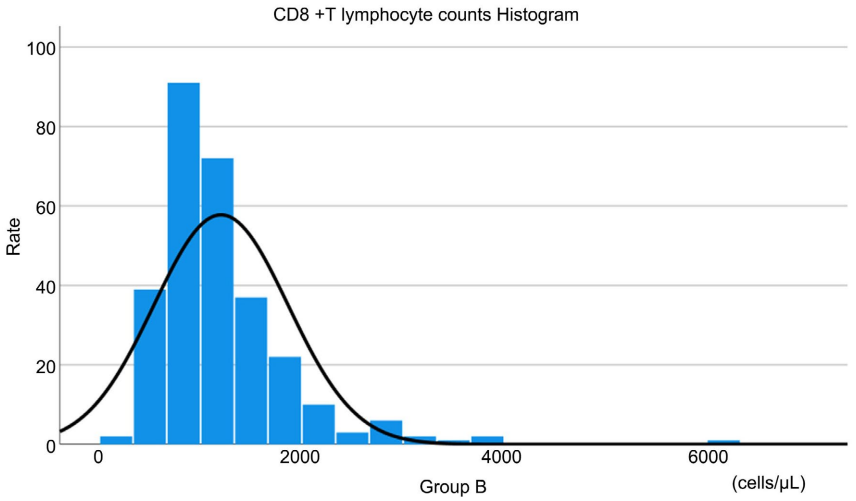


(b)

Figure 3. Two sets o f CD4+ T lymphocyte counts histogram and frequency distribution curve comparison

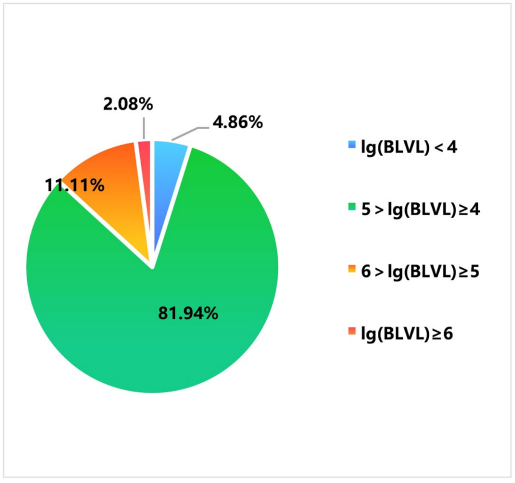


(a)

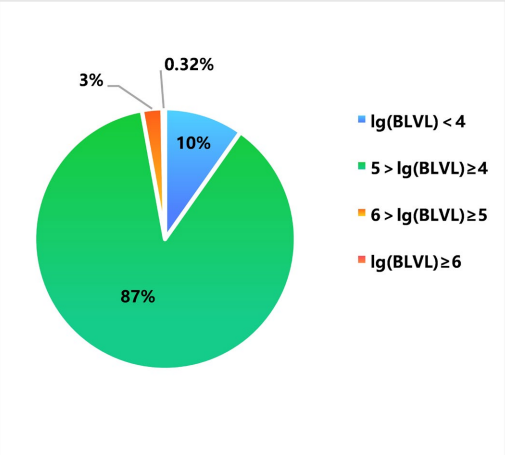


(b)

Figure 4. Two sets of CD8+ T lymphocyte counts histogram and frequency distribution curve comparison.



(a)



(b)

Figure 5. BLVL (lg) Variable frequency proportion.

4.2. Results of Logistic Regression Analysis

The above statistically significant indicators from groups A and B were included in the binary logistic regression analysis. Since the CD4/CD8 ratio is directly generated from CD4+ T lymphocyte count and CD8+ T lymphocyte count, the CD4/CD8 ratio was excluded to avoid influencing the experimental data. After multiple iterations of binary logistic regression analysis, the results showed statistically significant differences in HDL-c, CD8+ T lymphocyte levels, and baseline viral load (Table 2). HDL-c (OR = 3.817, 95% CI (1.703, 8.555)) and CD8+ T lymphocyte levels (OR = 1.003, 95% CI (1.002, 1.004)) were both positively correlated with CD4+ T lymphocyte levels, while BLVL (lg) was negatively correlated with CD4+ T lymphocyte levels (OR = 0.558, 95% CI (0.359, 0.868)).

Table 2. Logistic regression analysis results.

	B	Wald	P-value	Exp (B)	EXP (B) Lower limit of 95% CI	EXP (B) 95% CI upper limit
CD8 (per μL)	0.003	61.618	<0.01	1.003	1.002	1.004
HDL (mmol/L)	0.412	10.588	<0.01	3.817	1.703	8.555
BLVL (lg)	−0.583	6.686	0.01	0.558	0.359	0.868

4.3. ROC Diagnostic Curve

The ROC curve relationships between HDL-c, CD8+ T lymphocyte levels, CD4/CD8 ratio, BLVL (lg), and CD4+ T cell count levels (defined as CD4+ T cell count ≥ 200 cells/μL) are shown in Figure 6. Using the Youden index, the optimal cutoff values were determined as follows: HDL at 1.015 mmol/L (AUC 0.596), CD8+ T lymphocyte count at 747.5 cells/μL (AUC 0.800), and CD4/CD8 ratio at 0.283 (AUC 0.829), which yielded the largest AUC under the curve. Since BLVL (lg) negatively correlated with CD4+ T cell count, the area above the curve was used

for diagnostic value assessment, showing an optimal value of 4.39 (AUC 0.562). Among these four parameters, the CD4/CD8 ratio demonstrated the highest diagnostic value.

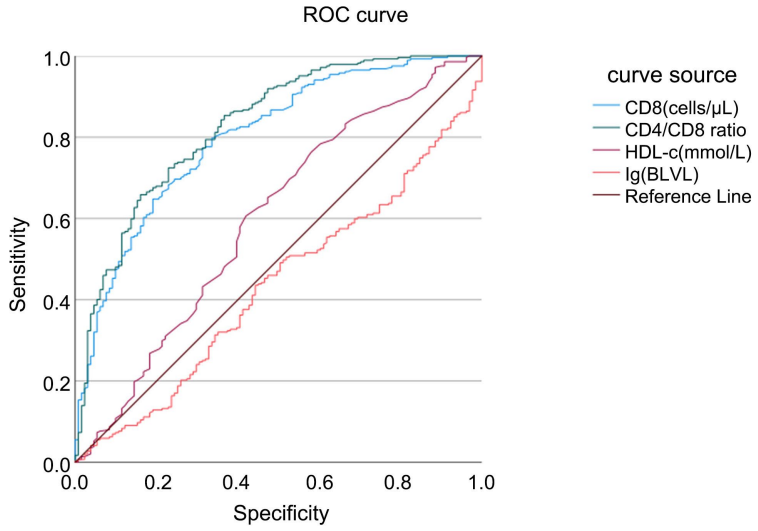


Figure 6. Schematic diagram of ROC curves of each index and CD4+T cell count level.

5. Discussion

The number of HIV-infected patients is currently increasing year by year, and it is not uncommon for HIV patients to have metabolic disorders such as lipid and blood sugar abnormalities. According to a meta-analysis by Derara Girma [9], approximately 21.7% of HIV-infected individuals in Ethiopia have metabolic syndrome, and about 21.01% of HIV-infected people in sub-Saharan Africa have metabolic syndrome [10]. The prevalence of dyslipidemia among HIV patients is higher than that in the general population, and the relationship between lipid metabolism and CD4+ T lymphocytes in HIV patients has gradually become a research hotspot in recent years.

In this study, HIV-infected individuals show varying educational levels, with the majority having a high school education or below. This is closely related to how cultural factors influence people's understanding of HIV transmission routes. Generally, those with higher education levels have better knowledge of HIV transmission routes. Among the transmission routes, people have sex with same gender contact accounts for 39.83%, particularly anal sex between men, which can easily damage rectal mucosa and poses a high risk for HIV transmission.

The CD4/CD8 ratio has always been an important indicator for predicting the prognosis of AIDS patients, especially in HIV-infected populations with CD4+ T lymphocytes < 200 cells/μL. In this group, patients with lower CD4/CD8 ratios have higher rates of opportunistic infections and mortality compared to patients with CD4+ T cells ≥ 200 cells/μL [4] [11]. A lower CD4/CD8 ratio typically indicates lower levels of CD4+ T lymphocytes, which corresponds to a poorer prognosis for patients. In this study, CD8+ T cell counts were positively correlated with

CD4+ T lymphocyte levels. According to a cell dynamics study by Payal Rana [12], increased activated CD8+ T lymphocytes can help maintain HIV infection at a stable phase. Additionally, in untreated HIV-infected individuals, cytotoxic CD8+ T cells can limit viral replication in lymphoid tissue cells [13]. This may be related a key epigenetic regulatory factor impact of histone deacetylase 1 (HDAC1) on CD8+ T cell differentiation. The absence of HDAC1 leads to the expansion of alternative Tex subsets with high expression of T cell exhaustion markers, resulting in increased viral load [14]. The results of this study showed that viral load was negatively correlated with CD4+ T cell levels [15]-[17], which is related to the direct killing of CD4+ T lymphocytes by the virus, induction of apoptosis, and mediation of cytotoxic effects.

In this study, HDL-c levels increase with the elevation of CD4+ T lymphocyte levels. Studies have shown that HIV-infected individuals have lower HDL-c levels compared to those uninfected with HIV [18]. Moreover, as the CD4+ T lymphocyte levels decrease and viral load increases, there is a corresponding decrease in high-density lipoprotein (HDL) levels [19]. HDL-c is an important indicator for assessing the severity of illness in untreated HIV-infected patients [20]. Among untreated antiretroviral populations, the CD4+ T lymphocyte level shows a negative correlation with the TG/HDL-c ratio [21], may be related to intestinal barrier dysfunction and macrophage activation affecting lipid metabolism in HIV-infected patients [22]. Additionally, studies suggest that HDL-c particles act as a protective barrier against HIV entry into infected cells by reducing gp41 expression [23]. The research results of Xiaorui Li [24] in China also show that high-density lipoprotein has important value in predicting CD4+ T lymphocyte levels in HIV infected individuals. However, through the aforementioned comparative results, HDL-c still has limitations in reflecting CD4+ T lymphocyte levels. Its diagnostic value is lower than that of the CD4/CD8 ratio and CD8+ T cells, which may be related to the direct influence of CD8+ T cell levels on human immune function and their synergistic effect on CD4+ T lymphocyte growth [25].

6. Conclusions

According to the results of this study, there is a certain correlation between HDL-c and CD4+ T lymphocyte levels. HDL and CD8+ T lymphocyte levels are positively correlated with CD4+ T lymphocyte levels, while BLVL is negatively correlated with CD4+ T lymphocyte levels. However, in the ROC diagnostic curve analysis model, the CD4/CD8 ratio demonstrated greater predictive value for evaluating CD4+ lymphocyte levels compared to HDL-c, baseline viral load levels, and CD8+ T lymphocyte counts. Nevertheless, the limited inclusion of data may introduce bias into the final results. Therefore, the results of this study indicate that HDL-c has limited diagnostic value as an independent predictor for CD4+ T lymphocytes. Due to limited patient numbers and single-center study factors, and current co-infections, and inflammatory markers, the existing data has certain limitations, future studies should incorporate more case data and relevant laboratory

test results to further validate.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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